



# **STIC Search Report**

## **Biotech-Chem Library**

**STIC Database Tracking Number: 198954**

**TO: Shailendra Kumar**  
**Location: rem-5c03/5c18**  
**Art Unit: 1621**  
**Monday, August 21, 2006**  
**Case Serial Number: 10/517581**

**From: Usha Shrestha**  
**Location: Biotech-Chem Library**  
**REM-1A64**  
**Phone: (571)272-3519**

**Usha.shrestha@uspto.gov**

### **Search Notes**

Examiner Kumar,

See attached results.

If you have any questions about this search feel free to contact me at any time.

Thank you for using STIC search services!

Usha Shrestha  
Technical Information Specialist  
STIC Biotech/Chem Library  
(571)272-3519

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ACCESS DB #  
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## Scientific and Technical Information Center

## SEARCH REQUEST FORM

Requester's Full Name: S. Kumar Examiner #: 69594 Date: 8/17/06  
Art Unit: 1621 Phone Number: 2-0640 Serial Number: 10517581  
Location (Bldg/Room#): REM (Mailbox #): 503 Results Format Preferred (circle): PAPER DISK  
\*\*\*\*\*  
503

To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following:

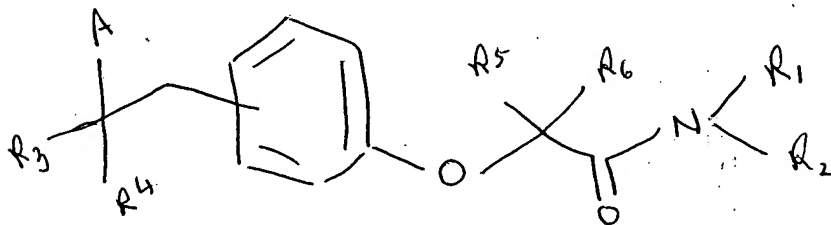
Title of Invention: Amide linker peroxisome proliferator activated receptor  
Inventors (please provide full names): Rafael Ferritto Crespo et al.

Earliest Priority Date: 6/19/02

## Search Topic:

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known.

\*For Sequence Searches Only\* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.



R<sup>1</sup> H  
R<sup>2</sup> alkyl etc.  
R<sup>3</sup> H, alkyl etc.  
R<sup>4</sup> is H, halo, alkyl etc.  
R<sup>5</sup> & R<sup>6</sup> H, alkyl etc.  
A is (CH<sub>2</sub>)<sub>m</sub> C=O R<sup>14</sup> C<sub>1</sub>-C<sub>3</sub> alkyl nitrile etc.

## STAFF USE ONLY

Searcher: un

Searcher Phone #: \_\_\_\_\_

Searcher Location: \_\_\_\_\_

Date Searcher Picked Up: 8/18/06Date Completed: 8/21/06Searcher Prep & Review Time: 60Online Time: 200

## Type of Search

\_\_\_\_ NA Sequence (#)

\_\_\_\_ AA Sequence (#)

2 Structure (#)

\_\_\_\_ Bibliographic

\_\_\_\_ Litigation

\_\_\_\_ Fulltext

\_\_\_\_ Other

## Vendors and cost where applicable

8109-11 STN \_\_\_\_\_ Dialog

\_\_\_\_ Questel/Orbit \_\_\_\_\_ Lexis/Nexis

\_\_\_\_ Westlaw \_\_\_\_\_ WWW/Internet

\_\_\_\_ In-house sequence systems

\_\_\_\_ Commercial \_\_\_\_\_ Oligomer \_\_\_\_\_ Score/Length  
\_\_\_\_ Interference \_\_\_\_\_ SPDI \_\_\_\_\_ Encode/Transl  
\_\_\_\_ Other (specify)

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FILE 'HCAPLUS' ENTERED AT 08:39:36 ON 21 AUG 2006

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SEL RN

FILE 'REGISTRY' ENTERED AT 08:39:59 ON 21 AUG 2006

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L6 19 S L5  
L7 1 S L2 AND L6  
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L10 135 S L9 AND L2  
SAV L9 KUM581/A  
L11 23 S L8 SAM SUB=L9  
L12 433 S L8 FUL SUB=L9  
SAV L12 KUM581A/A

FILE 'HCAPLUS' ENTERED AT 11:12:55 ON 21 AUG 2006

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L21 10 S L20 AND PEROXISOM?  
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L23 11 S L22 AND (1840-2002)/PRY,AY,PY  
L24 15 S L17 OR L23  
L25 14 S L24 NOT L1  
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L27 353 S L26(L) PREP/RL  
L28 156 S L27 AND BSU/RL  
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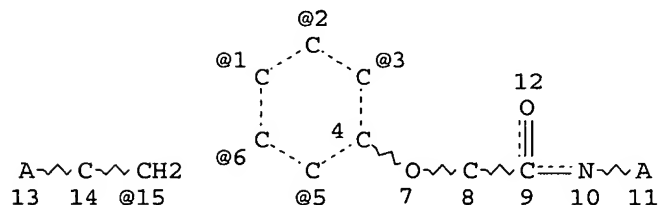
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STR



VPA 15-3/2/1/5/6 U

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NSPEC IS RC AT 13

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DEFAULT ECLEVEL IS LIMITED

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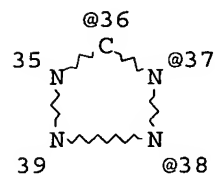
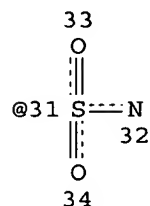
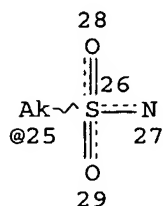
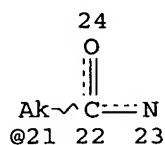
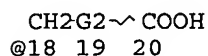
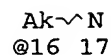
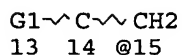
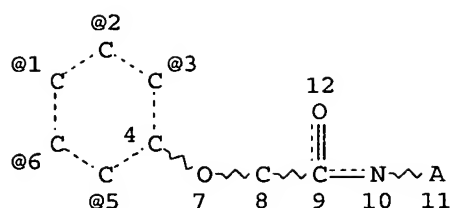
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NUMBER OF NODES IS 15

STEREO ATTRIBUTES: NONE

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 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:  
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 NUMBER OF NODES IS 38

STEREO ATTRIBUTES: NONE

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 L16 57 SEA FILE=HCAPLUS ABB=ON L14 NOT L15  
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L33 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:2837 HCAPLUS

DOCUMENT NUMBER: 140:59411

TITLE: Preparation of phenoxyalkanamides as amide  
 linker peroxisome proliferator activated  
 receptor agonists for treating and/or  
 preventing diabetes mellitus and syndrome X

INVENTOR(S): Ferritto Crespo, Rafael; Martin, Jose Alfredo;  
 Martin-Ortega, Finger Maria Dolores; Rojo  
 Garcia, Isabel; Shen, Quanrong; Warshawsky,  
 Alan M.; Xu, Yanping

PATENT ASSIGNEE(S): Eli Lilly and Company, USA

SOURCE: PCT Int. Appl., 168 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

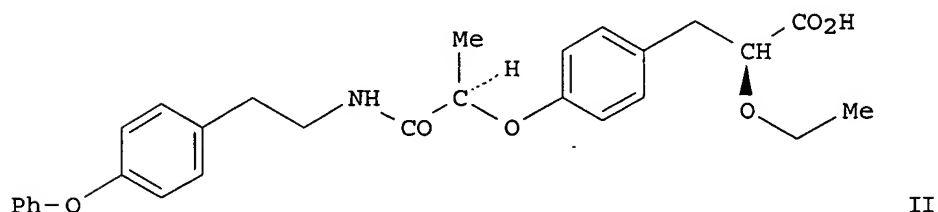
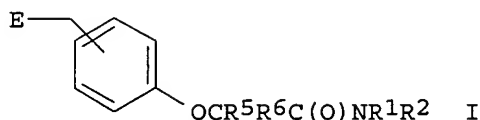
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004000789	A1	20031231	WO 2003-US16207	2003 0611
WO 2004000789	C2	20040311		
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CA 2488972	AA	20031231	CA 2003-2488972	2003 0611
AU 2003241579	A1	20040106	AU 2003-241579	2003

EP 1517882	A1	20050330	EP 2003-731326	0611
				2003
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CN 1662487	A	20050831	CN 2003-814173	2003
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US 2006111406	A1	20060525	US 2004-517581	2004
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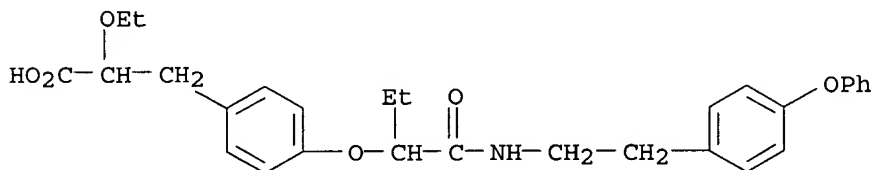
OTHER SOURCE(S): MARPAT 140:59411  
GI



AB The present invention is directed to phenoxyalkanamides (shown as I; variables defined below; e.g. II), compns., and their use as peroxisome proliferator activated receptor agonists for treating and/or preventing diabetes mellitus and syndrome X. The binding and cotransfection efficacy values found for compds. of this invention that are useful for modulating a PPAR $\alpha$  receptor are about <100 nM and >50%, resp. Although the methods of preparation are not claimed, .apprx.140 example preps. of I are included. For example, II was prepared in 3 steps starting from

(2S)-2-ethoxy-3-(4-hydroxyphenyl)propionic acid Me ester, (2S)-2-hydroxypropionic acid benzyl ester and involving intermediates (2S)-3-[4-[[[(1R)-1-[(benzyloxy)carbonyl]ethyl]oxy]phenyl]-2-ethoxypropionic acid Et ester and (2S)-3-[4-[[[(1R)-1-carboxyethyl]oxy]phenyl]-2-ethoxypropionic acid. For I: R1 = H, C1-C8 alkyl, C3-C6 cycloalkyl, aryl-C0-4-alkyl, heteroaryl-C0-4-alkyl, aminoC1-C4alkyl, C3-C6 cycloalkylaryl-C0-2-alkyl, arylheteroC1-C8alkyl, -CHC(O)C1-C4 alkoxy, C0-4-alkyl-C(O)heteroC1-C8alkyl, and -CH2C(O)-R15R16. R2 = C1-C8 alkyl, C3-C6 cycloalkyl, aryl-C0-C4-alkyl, heteroaryl-C0-C4-alkyl, heteroC1-C6cycloalkylaryl, heteroC1-C6cycloalkylarylC1-C4alkyl, aminoC1-C4alkyl, C3-C6 cycloalkylaryl-C0-C2-alkyl, arylheteroC1-C8alkyl, C0-C4-alkyl-C(O)heteroC1-C8alkyl, -CH(C(O)OCH3)benzyl, and -CH2C(O)R15''R16''. R1 and R2 together may form a heterocyclic ring which heterocyclic ring is (un)substituted with 1-3 substituents R1' and which heterocyclic ring is optionally fused with an aryl; E = C(R3)(R4)A, (CH2)nCOOR13, aryl-C0-C4-alkyl, thio-C1-C4-alkyl, thioaryl, arylC1-C4alkoxy, C1-C4alkoxy C1-C4alkyl, aminoaryl, and aminoC1-C4alkyl. R5 and R6 = H, C1-C8 alkyl, aryl-C0-C4-alkyl, heteroaryl-C0-C4-alkyl, C3-C6 cycloalkyl, aryl-C0-C2-alkyl, C3-C6 cycloalkyl-C0-2-alkyl, and -CH2C(O)R17R18.

- IT 638190-57-5P, 2-Ethoxy-3-[4-[1-[[2-(4-phenoxyphenyl)ethyl]carbamoyl]propoxy]phenyl]propionic acid (drug candidate, single diastereomer; preparation of phenoxyalkanamides as amide linker peroxisome proliferator activated receptor agonists for treating and/or preventing diabetes mellitus and syndrome X)
- RN 638190-57-5 HCAPLUS
- CN Benzenepropanoic acid,  $\alpha$ -ethoxy-4-[1-[[2-(4-phenoxyphenyl)ethyl]amino]carbonyl]propoxy]- (9CI) (CA INDEX NAME)



- IC ICM C07C235-20
- ICS C07C235-22; C07C235-24; C07D295-18; C07C235-26; C07C235-34; C07C233-18; C07C069-734; C07C323-41; C07D333-20; C07D211-32; C07D217-06; C07D317-58; C07D277-82; C07D213-40; C07D285-12; C07D277-46; A61K031-16; A61K031-425; A61K031-495
- CC 25-19 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
- Section cross-reference(s): 1, 63
- IT 638190-57-5P, 2-Ethoxy-3-[4-[1-[[2-(4-phenoxyphenyl)ethyl]carbamoyl]propoxy]phenyl]propionic acid (drug candidate, single diastereomer; preparation of phenoxyalkanamides as amide linker peroxisome proliferator activated receptor agonists for treating and/or preventing diabetes mellitus and syndrome X)
- IT 638190-05-3P, 2-Methoxy-3-[3-[(4-phenoxyphenyl)carbamoyl]methoxy]phenyl]propionic acid (drug candidate, single enantiomer; preparation of phenoxyalkanamides as amide linker peroxisome proliferator

activated receptor agonists for treating and/or preventing diabetes mellitus and syndrome X)

IT 638189-66-9P, (2S)-2-Ethoxy-3-[4-[[[(1R)-1-[[2-(4-phenoxyphenyl)ethyl]carbamoyl]ethyl]oxy]phenyl]propionic acid  
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638189-70-5P, (2S)-2-Ethoxy-3-[4-[[[(1R)-1-[[2-(4-trifluoromethylphenyl)ethyl]carbamoyl]ethyl]oxy]phenyl]propionic acid  
638189-71-6P, (2S)-2-Ethoxy-3-[4-[[[(1R)-1-[[2-(2-ethoxyphenyl)ethyl]carbamoyl]ethyl]oxy]phenyl]propionic acid  
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638189-75-0P, (2S)-3-[4-[[[(1R)-1-[[2-(3-Chlorophenyl)ethyl]carbamoyl]ethyl]oxy]phenyl]-2-ethoxypropionic acid  
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638189-91-0P, (2S)-2-Methoxy-3-[4-[[[(1S)-1-(naphthalen-1-yl)ethyl]carbamoyl]methoxy]phenyl]propionic acid  
638189-92-1P, (2S)-2-Methoxy-3-[4-[[[(1R)-1-phenylethyl]carbamoyl]methoxy]phenyl]propionic acid  
638189-93-2P, (2S)-2-Methoxy-3-[4-[[[methyl((1S)-1-phenylethyl)carbamoyl]methoxy]phenyl]propionic acid  
638189-94-3P, (2S)-3-[4-[2-[4-(4-Fluorobenzoyl)piperidin-1-yl]-2-oxoethoxy]phenyl]-2-methoxypropionic acid 638189-95-4P, (2S)-3-[4-[2-[4-(4-Chlorobenzoyl)piperidin-1-yl]-2-oxoethoxy]phenyl]-2-methoxypropionic acid 638189-96-5P, (2S)-2-Methoxy-3-[4-[[[(1R)-1-(methoxycarbonyl)-2-phenylethyl]carbamoyl]methoxy]phenyl]propionic acid

638189-97-6P, (2S)-3-[4-[2-[4-[(4-Chlorophenyl)phenylmethyl]piperazin-1-yl]-2-oxoethoxy]phenyl]-2-methoxypropionic acid  
**638189-98-7P**, (2S)-3-[4-[[[(4-Chlorophenyl)phenylmethyl]carbamoyl]methoxy]phenyl]-2-methoxypropionic acid **638189-99-8P** **638190-00-8P**, (2S)-3-[4-[(3,3-Diphenylpropylcarbamoyl)ethoxy]phenyl]-2-methoxypropionic acid **638190-01-9P**, (2S)-3-[4-[[Benzyl[2-(ethoxycarbonyl)ethyl]carbamoyl]methoxy]phenyl]-2-methoxypropionic acid **638190-02-0P**, (2S)-2-Methoxy-3-[4-[[[3-[(methyl)(phenyl)amino]propyl]carbamoyl]methoxy]phenyl]propionic acid **638190-03-1P**, (2S)-2-Methoxy-3-[4-[[[2-(4-methoxyphenoxy)ethyl]carbamoyl]methoxy]phenyl]propionic acid **638190-04-2P**, (2S)-2-Methoxy-3-[4-[(4-phenoxyphenylcarbamoyl)ethoxy]phenyl]propionic acid **638190-06-4P**, (2S)-2-Methoxy-3-[4-[1-methyl-1-[[2-(4-phenoxyphenyl)ethyl]carbamoyl]ethoxy]phenyl]propionic acid **638190-07-5P**, (2S)-3-[4-[1-[[2-(2-Ethoxyphenyl)ethyl]carbamoyl]-1-methylethoxy]phenyl]-2-methoxypropionic acid **638190-08-6P**, 2-Methoxy-2-methyl-3-[4-[[[2-(4-phenoxyphenyl)ethyl]carbamoyl]methoxy]phenyl]propionic acid **638190-10-0P**, (2S)-2-Methoxy-3-[4-[1-methyl-1-[[2-(3-trifluoromethylphenyl)ethyl]carbamoyl]ethoxy]phenyl]propionic acid **638190-11-1P**, (2S)-2-Methoxy-3-[4-[1-methyl-1-(3-trifluoromethylbenzylcarbamoyl)ethoxy]phenyl]propionic acid **638190-12-2P** **638190-13-3P**, (2S)-3-[4-[1-[[[Biphenyl-3-yl)methyl]carbamoyl]-1-methylethoxy]phenyl]-2-methoxypropionic acid **638190-14-4P**, (2S)-3-[4-[1-[[2-(2,5-Dimethoxyphenyl)ethyl]carbamoyl]-1-methylethoxy]phenyl]-2-methoxypropionic acid **638190-15-5P**, (2S)-3-[4-[1-[[2-(2-Fluorophenyl)ethyl]carbamoyl]-1-methylethoxy]phenyl]-2-methoxypropionic acid **638190-16-6P**, (2S)-2-Ethoxy-3-[4-[1-methyl-1-[[2-(3-trifluoromethylphenyl)ethyl]carbamoyl]ethoxy]phenyl]propionic acid **638190-19-9P**, (2S)-2-Ethoxy-3-[4-[1-(3-fluoro-5-trifluoromethylbenzylcarbamoyl)-1-methylethoxy]phenyl]propionic acid **638190-20-2P**, (2S)-3-[4-[1-[[2-(2-Chlorophenyl)ethyl]carbamoyl]-1-methylethoxy]phenyl]-2-ethoxypropionic acid **638190-21-3P**, (2S)-3-[4-[1-[[[Biphenyl-3-yl)methyl]carbamoyl]-1-methylethoxy]phenyl]-2-ethoxypropionic acid **638190-22-4P**, (2S)-3-[4-[1-[[2-(3-Chlorophenyl)ethyl]carbamoyl]-1-methylethoxy]phenyl]-2-ethoxypropionic acid **638190-23-5P**, (2S)-3-[4-[1-[[2-(2,5-Dimethoxyphenyl)ethyl]carbamoyl]-1-methylethoxy]phenyl]-2-ethoxypropionic acid **638190-24-6P**, (2S)-2-Ethoxy-3-[4-[1-[[2-(2-fluorophenyl)ethyl]carbamoyl]-1-methylethoxy]phenyl]propionic acid **638190-27-9P**, (2S)-3-[3-[1-[[2-(4-Ethylphenyl)ethyl]carbamoyl]-1-methylethoxy]phenyl]-2-methoxypropionic acid **638190-28-0P**, (2S)-2-Methoxy-3-[3-[1-methyl-1-[[2-(4-phenoxyphenyl)ethyl]carbamoyl]ethoxy]phenyl]propionic acid **638190-29-1P**, (2S)-3-[3-[1-(3-Fluoro-5-trifluoromethylbenzylcarbamoyl)-1-methylethoxy]phenyl]-2-methoxypropionic acid **638190-30-4P**, (2S)-3-[3-[1-[[[Biphenyl-3-yl)methyl]carbamoyl]-1-methylethoxy]phenyl]-2-methoxypropionic acid **638190-31-5P**, (2S)-3-[3-[1-[[2-(3-Chlorophenyl)ethyl]carbamoyl]-1-methylethoxy]phenyl]-2-methoxypropionic acid **638190-32-6P**, (2S)-2-Methoxy-3-[4-[[[(1S)-1-phenylethyl]carbamoyl]methoxy]phenyl]propionic acid **638190-33-7P**, (2S)-3-[3-[1-[[2-(2,4-Dichlorophenyl)ethyl]carbamoyl]-1-methylethoxy]phenyl]-2-methoxypropionic acid **638190-34-8P**, (2S)-3-[3-[1-[[2-



(2,6-Dichlorophenyl)ethyl] carbamoyl]-1-methylethoxy]phenyl]-2-methoxypropionic acid **638190-35-9P**, (2S)-3-[3-(1-Heptylcarbamoyl-1-methylethoxy)phenyl]-2-methoxypropionic acid **638190-36-0P**, (2S)-3-[4-[1-[[2-(2,4-Dichlorophenyl)ethyl] carbamoyl]-1-methylethoxy]phenyl]-2-methoxypropionic acid **638190-37-1P**, (2S)-3-[4-[1-[[2-(2,4-Dichlorophenyl)ethyl] carbamoyl]-1-methylethoxy]phenyl]-2-ethoxypropionic acid **638190-38-2P**, (2S)-3-[4-[1-[[2-(2,6-Dichlorophenyl)ethyl] carbamoyl]-1-methylethoxy]phenyl]-2-ethoxypropionic acid **638190-39-3P**, (2S)-2-Ethoxy-3-[4-[1-[[2-(4-ethylphenyl)ethyl] carbamoyl]-1-methylethoxy]phenyl]propionic acid **638190-40-6P**, (2S)-2-Ethoxy-3-[4-[1-[[2-(2-ethoxyphenyl)ethyl] carbamoyl]-1-methylethoxy]phenyl]propionic acid **638190-41-7P**, (2S)-2-Ethoxy-3-[4-(1-heptylcarbamoyl-1-methylethoxy)phenyl]propionic acid **638190-46-2P**, (2S)-3-[4-[[[(1S)-1-[[2-(2-Chlorophenyl)ethyl] carbamoyl]ethyl]oxy]phenyl]-2-ethoxypropionic acid **638190-47-3P**, (2S)-2-Ethoxy-3-[4-[[[(1S)-1-(hexylcarbamoyl)ethyl]oxy]phenyl]propionic acid **638190-48-4P**, (2S)-2-Ethoxy-3-[4-[[[(1S)-1-(3-trifluoromethylbenzylcarbamoyl)ethyl]oxy]phenyl]propionic acid **638190-49-5P**, (2S)-2-Ethoxy-3-[4-[[[(1S)-1-(5-fluoro-3-trifluoromethylbenzylcarbamoyl)ethyl]oxy]phenyl]propionic acid **638190-50-8P**, (2S)-2-Ethoxy-3-[4-[[[(1S)-1-(3-phenylbenzylcarbamoyl)ethyl]oxy]phenyl]propionic acid **638190-51-9P**, (2S)-2-Ethoxy-3-[4-[[[(1S)-1-[[2-(4-phenoxyphenyl)ethyl] carbamoyl]ethyl]oxy]phenyl]propionic acid **638190-52-0P**, (2S)-2-Ethoxy-3-[4-[[[(1S)-1-[[2-(3-trifluoromethylphenyl)ethyl] carbamoyl]ethyl]oxy]phenyl]propionic acid **638190-53-1P**, (2S)-3-[4-[[[(1S)-1-[[2-(2,6-Dichlorophenyl)ethyl] carbamoyl]ethyl]oxy]phenyl]-2-ethoxypropionic acid **638190-54-2P**, (2S)-2-Ethoxy-3-[4-[[[(1S)-1-[[2-(4-ethylphenyl)ethyl] carbamoyl]ethyl]oxy]phenyl]propionic acid **638190-55-3P**, (2S)-2-Ethoxy-3-[4-[1-[[2-(4-ethylphenyl)ethyl] carbamoyl]propoxy]phenyl]propionic acid **638190-56-4P**, (2S)-2-Ethoxy-3-[4-[1-(hexylcarbamoyl)propoxy]phenyl]propionic acid **638190-58-6P**, (2S)-3-[4-[[[(1R)-Cyclohexyl[[2-(4-ethylphenyl)ethyl] carbamoyl]methyl]oxy]phenyl]-2-ethoxypropionic acid **638190-59-7P**, (2S)-2-Ethoxy-3-[4-[[[(1R)-1-[[2-(4-ethylphenyl)ethyl] carbamoyl]-2-phenylethyl]oxy]phenyl]propionic acid **638190-61-1P**, (2S)-2-Methyl-2-phenoxy-3-[4-[1-[[2-(4-phenoxyphenyl)ethyl] carbamoyl]methoxy]phenyl]propionic acid **638190-63-3P**, (2S)-2-Phenoxy-2-[4-[[[2-(4-phenoxyphenyl)ethyl] carbamoyl]methoxy]benzyl]butyric acid **638190-65-5P**, (2S)-2-Methyl-3-[4-[[[2-(4-phenoxyphenyl)ethyl] carbamoyl]methoxy]phenyl]-2-(4-trifluoromethoxyphenoxy)propionic acid **638190-67-7P**, (2S)-2-(4-Fluorophenoxy)-2-methyl-3-[4-[[[2-(4-phenoxyphenyl)ethyl] carbamoyl]methoxy]phenyl]propionic acid **638190-69-9P**, (2S)-3-[4-[[[(Biphenyl-4-yl)methyl] carbamoyl]methoxy]phenyl]-2-methoxypropionic acid **638190-70-2P**, (2S)-2-Methoxy-3-[4-[[methyl[(naphthalen-1-yl)methyl] carbamoyl]methoxy]phenyl]propionic acid **638190-71-3P**, (2S)-3-[4-[2-(4-Benzhydrylpiperazin-1-yl)-2-oxoethoxy]phenyl]-2-methoxypropionic acid **638190-72-4P**, (2S)-3-[4-[2-[4-[Bis(4-fluorophenyl)methyl]piperazin-1-yl)-2-oxoethoxy]phenyl]-2-methoxypropionic acid **638190-73-5P**, (2S)-2-Methoxy-3-[4-[[[2-(4-phenoxyphenyl)ethyl] carbamoyl]methoxy]phenyl]propionic acid **638190-74-6P**, (2S)-3-[4-[2-(3,4-Dihydro-1H-isoquinolin-2-

yl)-2-oxoethoxy]phenyl]-2-methoxypropionic acid  
**638190-75-7P**, (2S)-3-[4-[[[Benzyl](phenethyl)carbamoyl]methoxy]phenyl]-2-methoxypropionic acid **638190-76-8P**,  
 (2S)-3-[4-[2-[4-(4-Fluorophenyl)piperazin-1-yl]-2-oxoethoxy]phenyl]-2-methoxypropionic acid **638190-77-9P**,  
 (2S)-2-Methoxy-3-[4-[[[4-(4-chlorophenyl)-3-methylpiperazin-1-yl]carbonyl]methoxy]phenyl]propionic acid **638190-78-0P**,  
 (2S)-3-[4-[2-[4-(3-Chlorophenyl)piperazin-1-yl]-2-oxoethoxy]phenyl]-2-methoxypropionic acid **638190-79-1P**,  
 (2S)-3-[4-[2-[4-(4-Chlorobenzyl)piperazin-1-yl]-2-oxoethoxy]phenyl]-2-methoxypropionic acid **638190-80-4P**,  
 (2S)-3-[4-[2-[4-(2-Fluorophenyl)piperazin-1-yl]-2-oxoethoxy]phenyl]-2-methoxypropionic acid **638190-81-5P**,  
 (2S)-3-[4-[[[(Benzo[1,3]dioxol-5-yl)methyl]carbamoyl]methoxy]phenyl]-2-methoxypropionic acid **638190-82-6P**,  
 (2S)-3-[4-[[[2-(4-Bromophenyl)ethyl]carbamoyl]methoxy]phenyl]-2-methoxypropionic acid **638190-83-7P**, (2S)-2-Methoxy-3-[4-[[[naphthalen-1-yl)methyl]carbamoyl]methoxy]phenyl]propionic acid **638190-84-8P**, (2S)-3-[4-[[[2-[(2,6-Dichlorobenzyl)sulfanyl]ethyl]carbamoyl]methoxy]phenyl]-2-methoxypropionic acid **638190-85-9P**, (2S)-3-[4-[[[Benzyl[(1R)-1-phenylethyl]carbamoyl]methoxy]phenyl]-2-methoxypropionic acid **638190-86-0P**, (2S)-3-[4-[2-[4-(4-Acetylphenyl)piperazin-1-yl]-2-oxoethoxy]phenyl]-2-methoxypropionic acid **638190-87-1P**, (2S)-2-Methoxy-3-[4-[2-oxo-2-[4-(p-tolyl)piperazin-1-yl]ethoxy]phenyl]propionic acid **638190-88-2P**, (2S)-3-[4-[[Ethyl(2-fluorobenzyl)carbamoyl]methoxy]phenyl]-2-methoxypropionic acid **638190-89-3P**, (2S)-3-[4-[[Ethyl(3-methylbenzyl)carbamoyl]methoxy]phenyl]-2-methoxypropionic acid **638190-90-6P**, (2S)-3-[4-[2-[4-(4-Fluorobenzyl)piperazin-1-yl]-2-oxoethoxy]phenyl]-2-methoxypropionic acid **638190-91-7P**, (2S)-3-[4-[[[6-Fluorobenzothiazol-2-yl]carbamoyl]methoxy]phenyl]-2-methoxypropionic acid **638190-92-8P**, (2S)-3-[4-[[[2-(Ethyl-m-tolylamino)ethyl]carbamoyl]methoxy]phenyl]-2-methoxypropionic acid **638190-93-9P**, (2S)-2-Methoxy-3-[4-[[[2-(pyridin-2-yl)ethyl]carbamoyl]methoxy]phenyl]propionic acid **638190-94-0P**, (2S)-2-Methoxy-3-[4-[[[2-(pyridin-3-yl)ethyl]carbamoyl]methoxy]phenyl]propionic acid **638190-95-1P**, (2S)-3-[4-[[[trans-4-tert-Butylcyclohexyl]carbamoyl]methoxy]phenyl]-2-methoxypropionic acid **638190-96-2P**, (2S)-3-[4-[[[cis-4-tert-Butylcyclohexyl]carbamoyl]methoxy]phenyl]-2-methoxypropionic acid **638190-97-3P**, (2S)-3-[4-[(Cyclobutylcarbamoyl]methoxy]phenyl]-2-methoxypropionic acid **638190-98-4P**, (2S)-3-[4-[[[1,3-Dimethylbutylcarbamoyl]methoxy]phenyl]-2-methoxypropionic acid **638190-99-5P**, (2S)-2-Methoxy-3-[4-[[[1-methylhexylcarbamoyl]methoxy]phenyl]propionic acid **638191-00-1P**, (2S)-2-Methoxy-3-[4-[[[1-methylbutylcarbamoyl]methoxy]phenyl]propionic acid **638191-01-2P**, (2S)-2-Methoxy-3-[4-[[[3-methylbutylcarbamoyl]methoxy]phenyl]propionic acid **638191-02-3P**, (2S)-3-[4-[(Cyclopentylcarbamoyl]methoxy]phenyl]-2-methoxypropionic acid **638191-03-4P**, (2S)-2-Methoxy-3-[4-[[[1-methyl-3-phenylpropyl]carbamoyl]methoxy]phenyl]propionic acid **638191-04-5P**, (2S)-3-[4-[[[2,2,3,3,4,4,4-Heptafluorobutylcarbamoyl]methoxy]phenyl]-2-methoxypropionic acid **638191-05-6P**, (2S)-3-[4-[[[5-tert-Butyl-1,3,4]thiadiazol-2-yl]carbamoyl]methoxy]phenyl]-2-methoxypropionic acid **638191-06-7P**, (2S)-3-[4-[[[4-tert-

Butylthiazol-2-yl) carbamoyl]methoxy]phenyl]-2-methoxypropionic acid **638191-07-8P**, (2S)-3-[4-[[[5-Cyclopropyl-[1,3,4]thiadiazol-2-yl) carbamoyl]methoxy]phenyl]-2-methoxypropionic acid **638191-08-9P**, (2S)-3-[4-[[[Hexylcarbamoyl]methoxy]phenyl]-2-methoxypropionic acid **638191-09-0P**, (2S)-3-[4-[[[Heptylcarbamoyl]methoxy]phenyl]-2-methoxypropionic acid **638191-10-3P**, (2S)-3-[4-[[[3,3-Dimethylbutylcarbamoyl]methoxy]phenyl]-2-methoxypropionic acid **638191-11-4P**, 3-[3-[[[cis-4-tert-Butylcyclohexyl) carbamoyl]methoxy]phenyl]-2-methoxypropionic acid **638191-12-5P**, 3-[3-[[[trans-4-tert-Butylcyclohexyl) carbamoyl]methoxy]phenyl]-2-methoxypropionic acid **638191-13-6P**, 3-[4-[[[Heptylcarbamoyl]methoxy]phenyl]-2-methoxy-2-methylpropionic acid **638191-17-0P**, 2-Ethoxy-3-[4-[1-(3-trifluoromethylbenzylcarbamoyl)ethoxy]phenyl]propionic acid **638191-18-1P**, 2-Ethoxy-3-[4-[1-(5-fluoro-3-trifluoromethylbenzylcarbamoyl)ethoxy]phenyl]propionic acid **638191-19-2P**, 2-Ethoxy-3-[4-[1-[[3-phenylbenzyl) carbamoyl]ethoxy]phenyl]propionic acid **638191-20-5P**, 2-Ethoxy-3-[4-[1-[[2-(4-phenoxyphenyl)ethyl] carbamoyl]ethoxy]phenyl]propionic acid **638191-21-6P**, 2-Ethoxy-3-[4-[1-[[2-(3-trifluoromethylphenyl)ethyl] carbamoyl]ethoxy]phenyl]propionic acid **638191-22-7P**, 3-[4-[1-[[2-(2,6-Dichlorophenyl)ethyl] carbamoyl]ethoxy]phenyl]-2-ethoxypropionic acid **638191-23-8P**, 2-Ethoxy-3-[4-[1-[[2-(4-ethylphenyl)ethyl] carbamoyl]ethoxy]phenyl]propionic acid **638191-24-9P**, 3-[4-[Cyclohexyl[[2-(4-ethylphenyl)ethyl] carbamoyl]methoxy]phenyl]-2-ethoxypropionic acid **638191-25-0P**, 2-Ethoxy-3-[4-[1-[[2-(4-ethylphenyl)ethyl] carbamoyl]-2-phenylethoxy]phenyl]propionic acid **639010-29-0P**, (2S)-3-[4-[[[1R]-1-(4-tert-Butylcyclohexylcarbamoyl)ethyl]oxy]phenyl]-2-ethoxypropionic acid **639010-30-3P**, (2S)-3-[4-[1-(4-tert-Butylcyclohexylcarbamoyl)-1-methylethoxy]phenyl]-2-methoxypropionic acid **639010-31-4P**, (2S)-3-[3-[1-(4-tert-Butylcyclohexylcarbamoyl)-1-methylethoxy]phenyl]-2-methoxypropionic acid **639010-32-5P**, (2S)-3-[4-[[[1S]-1-(4-tert-Butylcyclohexylcarbamoyl)ethyl]oxy]phenyl]-2-ethoxypropionic acid

(drug candidate; preparation of phenoxyalkanamides as amide linker peroxisome proliferator activated receptor agonists for treating and/or preventing diabetes mellitus and syndrome X)

IT 23508-35-2P, (2S)-3-(4-Hydroxyphenyl)-2-hydroxypropionic acid  
 156335-14-7P, Methyl 3-(4-hydroxyphenyl)-2-methoxypropanoate  
 162919-37-1P, (2S)-3-[4-(Benzyloxy)phenyl]-2-hydroxypropionic acid  
 222835-03-2P, 3-[4-(Benzyloxy)phenyl]-2-ethoxyacrylic acid ethyl ester  
 222835-04-3P, 3-[4-(Benzyloxy)phenyl]-2-ethoxypropionic acid methyl ester  
 325793-76-8P, Propyl (2S)-3-(4-hydroxyphenyl)-2-ethoxypropionate  
 361576-28-5P, 3-[4-(Benzyloxy)phenyl]-2-ethoxy-3-hydroxypropionic acid ethyl ester  
 477979-20-7P, (2S)-3-(4-Hydroxyphenyl)-2-methoxypropionic acid ethyl ester  
 477980-43-1P 477982-28-8P, 3-(4-Hydroxyphenyl)-2-methoxypropanoic acid  
 481072-40-6P, Propyl (2S)-3-[4-(benzyloxy)phenyl]-2-hydroxypropionate  
 638189-56-7P 638189-58-9P, (2S)-3-[4-[[[tert-Butoxycarbonyl]methoxy]phenyl]-2-methoxypropionic acid ethyl ester  
 638189-59-0P, (2S)-3-[4-(Carboxymethoxy)phenyl]-2-methoxypropionic acid ethyl ester  
 638189-61-4P, 3-[3-[[[tert-Butoxycarbonyl]methoxy]phenyl]-2-methoxypropionic acid methyl ester  
 638189-62-5P,

3-[3-(Carboxymethoxy)phenyl]-2-methoxypropionic acid methyl ester  
638189-63-6P, (2S)-2-Methoxy-3-[4-[(1-methyl-1-octylcarbamoyl)ethoxy]phenyl]propionic acid 638189-64-7P,  
(2S)-3-[4-[1-(tert-Butoxycarbonyl)-1-methylethoxy]phenyl]-2-methoxypropionic acid ethyl ester 638189-65-8P 638189-67-0P,  
(2S)-3-[4-[(1R)-1-[(Benzyloxy)carbonyl]ethyl]oxy]phenyl]-2-ethoxypropionic acid ethyl ester 638189-68-1P,  
(2S)-3-[4-[(1R)-1-Carboxyethyl]oxy]phenyl]-2-ethoxypropionic acid ethyl ester 638190-17-7P, (2S)-3-[4-(1-Carboxy-1-methylethoxy)phenyl]-2-ethoxypropionic acid ethyl ester 638190-18-8P, (2S)-3-[4-[1-(tert-Butoxycarbonyl)-1-methylethoxy]phenyl]-2-ethoxypropionic acid ethyl ester 638190-25-7P, (2S)-3-[3-[1-(tert-Butoxycarbonyl)-1-methylethoxy]phenyl]-2-methoxypropionic acid methyl ester 638190-26-8P, (2S)-3-[3-(1-Carboxy-1-methylethoxy)phenyl]-2-methoxypropionic acid methyl ester 638190-42-8P,  
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638191-15-8P, Propyl (2S)-3-[4-(benzyloxy)phenyl]-2-ethoxypropionate 638191-16-9P, Propyl (2S)-3-[4-((1R)-1-carboxyethyl)phenyl]-2-ethoxypropionate

(preparation of phenoxyalkanamides as amide linker peroxisome proliferator activated receptor agonists for treating and/or preventing diabetes mellitus and syndrome X)

IT 638189-60-3P, 3-[3-[[[2-(4-Ethylphenyl)ethyl]carbamoyl]methoxy]phenyl]-2-methoxypropionic acid

(single enantiomer; preparation of phenoxyalkanamides as amide linker peroxisome proliferator activated receptor agonists for treating and/or preventing diabetes mellitus and syndrome X)

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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ACCESSION NUMBER: 2005:1335635 HCAPLUS

DOCUMENT NUMBER: 144:69628

TITLE: Preparation of phenoxyacetamide derivatives as modulators of peroxisome proliferator-activated receptors (PPAR)

INVENTOR(S): Alstermark, Eva-Lotte Lindstedt; Olsson, Anna Christina; Li, Lanna

PATENT ASSIGNEE(S): Swed.

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CODEN: USXXCO

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2004  
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2002  
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2003  
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ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP,  
KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,  
MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT,  
RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT,  
TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW  
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GN, GQ, GW, ML, MR, NE, SN, TD, TG

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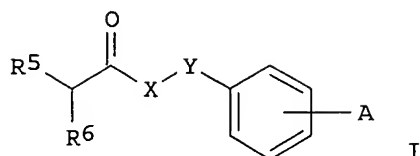
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OTHER SOURCE(S): MARPAT 144:69628  
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AB The phenyl-, phenoxy-, or phenylthioalkanamidetitle compds., (in particular phenoxyacetamide derivs.) (I) [A is situated in the ortho, meta or para position and represents CR3R4CR1R2COR, CR3:CR1COR (wherein R = H, alkyl, (un)substituted HO or NH2; R1 = alkyl, aryl, alkenyl, alkynyl, or when A is CR3R4CR1R2COR, R1 can also be cyano, (un)substituted HO, SH, OCONH2, SO2NH2, CO2H, etc.; R2 = H, halogen, alkyl, aryl, alkylaryl; R3, R4 = H, alkyl, aryl, alkylaryl]; Y = O, S, a single bond; n = an integer of 1-4; X = alkyl; R5, R6 = H, each (un)substituted C1-13 alkyl, C2-10 alkenyl, or C2-10 alkynyl; or R5, R6 = each (un)substituted C3-8 cycloalkyl, C3-C8 cycloalkenyl, aryl, heterocyclyl, or heteroaryl; or R5 and R6 together with the nitrogen atom to which they are attached form a single or a fused heterocyclic system] are prepared. These compds. are useful in treating clin. conditions including lipid disorders (dyslipidemias) whether or not associated with insulin resistance, and other manifestations of the metabolic syndrome. Thus, a solution of 0.598 g N-butyl-N-[2-fluoro-4-(trifluoromethyl)benzyl]amine and 0.593 g [4-((2S)-2,3-diethoxy-3-oxopropyl)phenoxy]acetic acid in 20 mL CH2Cl2 was treated with 0.80 mL N,N-diisopropylethylamine and 0.674 g O-(benzotriazol-1-yl)-N,N,N',N'-tetramethyluronium tetrafluoroborate and the reaction mixture was stirred at room temperature overnight to give, after workup and silica gel chromatog., 74% Et (2S)-3-[4-[2-[butyl[2-fluoro-4-(trifluoromethyl)benzyl]amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoate (II). A solution of 0.748 g II in 70 mL MeCN was treated with 35 mL 0.10 M LiOH and the reaction mixture was stirred at room temperature overnight, neutralized with 5% HCl, concentrated, acidified with 5% HCl, and extracted with EtOAc to give 97% (2S)-3-[4-[2-[butyl[2-fluoro-4-(trifluoromethyl)benzyl]amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoic acid (III). III showed EC50 of 0.001  $\mu$ mol/L for human PPAR $\alpha$ .

IT **549501-66-8P**, (2S)-3-[4-[2-[(Cyclohexylmethyl)(heptyl)amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoic acid **549501-72-6P**, (2S)-3-[4-[2-[(2,4-Difluorobenzyl)(heptyl)amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoic acid **549532-33-4P**, (2S)-3-[4-[2-[Benzyl(hexyl)amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoic acid **549532-35-6P**, (2S)-2-Ethoxy-3-[4-[2-[hexyl(2-phenylethyl)amino]-2-oxoethoxy]phenyl]propanoic acid **638189-90-9P** **638189-91-0P** **638189-93-2P** **638189-96-5P** **638189-98-7P** **638189-99-8P**

638190-00-8P, (2S)-4-[2-[(3,3-Diphenylpropyl)amino]-2-oxoethoxy]- $\alpha$ -methoxybenzenepropanoic acid  
638190-01-9P, (2S)-4-[2-[(3-Ethoxy-3-oxopropyl)(phenylmethyl)amino]-2-oxoethoxy]- $\alpha$ -methoxybenzenepropanoic acid 638190-02-0P  
638190-03-1P, (2S)- $\alpha$ -Methoxy-4-[2-[[2-(4-methoxyphenoxy)ethyl]amino]-2-oxoethoxy]benzenepropanoic acid  
638190-04-2P 638190-05-3P 638190-08-6P  
638190-32-6P 638190-61-1P 638190-62-2P  
638190-63-3P 638190-65-5P 638190-67-7P  
638190-69-9P, (2S)-4-[2-[[1,1'-Biphenyl-4-yl)methyl]amino]-2-oxoethoxy]- $\alpha$ -methoxybenzenepropanoic acid  
638190-70-2P, (2S)- $\alpha$ -Methoxy-4-[2-[methyl[(1-naphthalenyl)methyl]amino]-2-oxoethoxy]benzenepropanoic acid  
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, (2S)-4-[2-[(1,3-Benzodioxol-5-yl)methyl]amino]-2-oxoethoxy]- $\alpha$ -methoxybenzenepropanoic acid 638190-82-6P,  
(2S)-4-[2-[[2-(4-Bromophenyl)ethyl]amino]-2-oxoethoxy]- $\alpha$ -methoxybenzenepropanoic acid 638190-83-7P,  
(2S)- $\alpha$ -Methoxy-4-[2-[[1-naphthalenyl)methyl]amino]-2-oxoethoxy]benzenepropanoic acid 638190-84-8P,  
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(2S)-4-[2-[Ethyl[(3-methylphenyl)methyl]amino]-2-oxoethoxy]- $\alpha$ -methoxybenzenepropanoic acid 638190-92-8P,  
(2S)-4-[2-[[2-[Ethyl(3-methylphenyl)amino]ethyl]amino]-2-oxoethoxy]- $\alpha$ -methoxybenzenepropanoic acid  
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638190-94-0P, (2S)- $\alpha$ -Methoxy-4-[2-oxo-2-[[2-(3-pyridinyl)ethyl]amino]ethoxy]benzenepropanoic acid  
638190-95-1P 638190-96-2P 638190-97-3P  
, (2S)-4-[2-(Cyclobutylamino)-2-oxoethoxy]- $\alpha$ -methoxybenzenepropanoic acid 638190-98-4P  
638190-99-5P 638191-00-1P 638191-01-2P  
, (2S)- $\alpha$ -Methoxy-4-[2-[(3-methylbutyl)amino]-2-oxoethoxy]benzenepropanoic acid 638191-02-3P,  
(2S)-4-[2-(Cyclopentylamino)-2-oxoethoxy]- $\alpha$ -methoxybenzenepropanoic acid 638191-03-4P  
638191-04-5P, (2S)-4-[2-[(2,2,3,3,4,4,4-Heptafluorobutyl)amino]-2-oxoethoxy]- $\alpha$ -methoxybenzenepropanoic acid 638191-08-9P,  
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(2S)-4-[2-(Heptylamino)-2-oxoethoxy]- $\alpha$ -methoxybenzenepropanoic acid 638191-10-3P,  
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(2S)-3-[4-[2-[Butyl[2-fluoro-4-(trifluoromethyl)benzyl]amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoic acid 719277-14-2P,  
(2S)-3-[4-[2-[(4-Chlorobenzyl)(ethyl)amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoic acid 719277-15-3P, (2S)-2-Ethoxy-3-[4-[2-[ethyl[4-(trifluoromethoxy)benzyl]amino]-2-oxoethoxy]phenyl]propanoic acid 719277-16-4P,



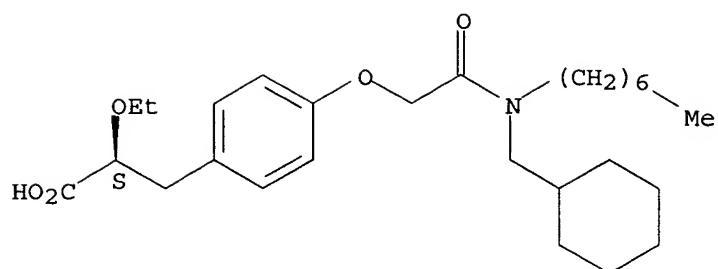
(2S)-2-Ethoxy-3-[4-[2-[ethyl[4-(trifluoromethyl)benzyl]amino]-2-oxoethoxy]phenyl]propanoic acid **719277-17-5P**,  
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 (2S)-3-[4-[2-[(2,3-Dimethoxybenzyl)(heptyl)amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoic acid **816465-23-3P**,  
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 (2S)-2-Ethoxy-3-[4-[2-[ethyl(2-fluorobenzyl)amino]-2-oxoethoxy]phenyl]propanoic acid **816465-35-7P**,  
 (2S)-3-[4-[2-[(4-(Benzyloxy)benzyl)(butyl)amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoic acid **816465-37-9P**,  
 (2S)-3-[4-[2-[Bis(4-Chlorobenzyl)amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoic acid **816465-43-7P**, (2S)-3-[4-[2-[(4-tert-Butylbenzyl)(4-chlorobenzyl)amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoic acid **816465-47-1P**, (2S)-3-[4-[2-[(4-Chlorobenzyl)[4-(trifluoromethyl)benzyl]amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoic acid **816465-51-7P**,  
 (2S)-3-[4-[2-[Bis[4-(Trifluoromethyl)benzyl]amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoic acid **816465-55-1P**,  
 (2S)-3-[4-[2-[Benzyl(ethyl)amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoic acid **816465-57-3P**, (2S)-3-[4-[2-[(4-tert-Butylbenzyl)(ethyl)amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoic acid **816465-64-2P**, (2S)-4-[2-(Heptylamino)-2-oxoethoxy]- $\alpha$ -methoxy- $\alpha$ -methylbenzenepropanoic acid **816465-67-5P**, (2S)-3-[2-[[2-(4-Ethylphenyl)ethyl]amino]-2-oxoethoxy]- $\alpha$ -methoxybenzenepropanoic acid **817181-62-7P 871731-30-5P**

(preparation of phenoxyacetamide derivs. as modulators of  
 peroxisome proliferator-activated receptors for  
 treating metabolic disorder)

RN 549501-66-8 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[(cyclohexylmethyl)heptylamino]-2-oxoethoxy]- $\alpha$ -ethoxy-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

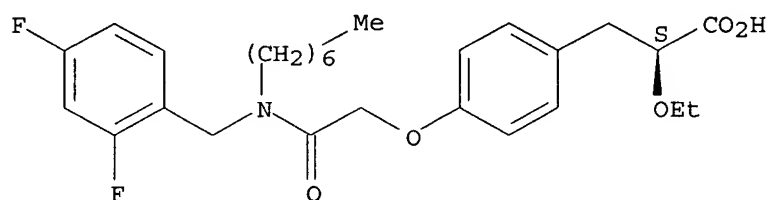
Absolute stereochemistry.



RN 549501-72-6 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[2-(4-difluorophenyl)methyl]heptylamino]-2-oxoethoxy]-α-ethoxy-, (αS)- (9CI) (CA INDEX NAME)

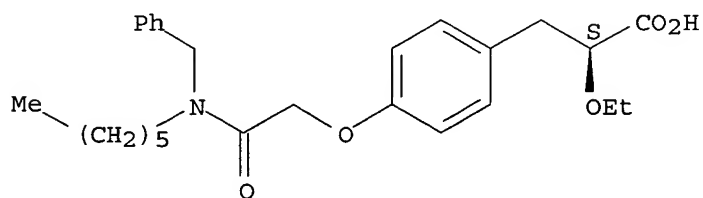
Absolute stereochemistry.



RN 549532-33-4 HCAPLUS

CN Benzenepropanoic acid, α-ethoxy-4-[2-[hexyl(phenylmethyl)amino]-2-oxoethoxy]-, (αS)- (9CI) (CA INDEX NAME)

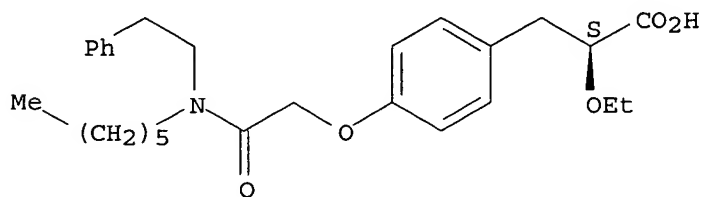
Absolute stereochemistry.



RN 549532-35-6 HCAPLUS

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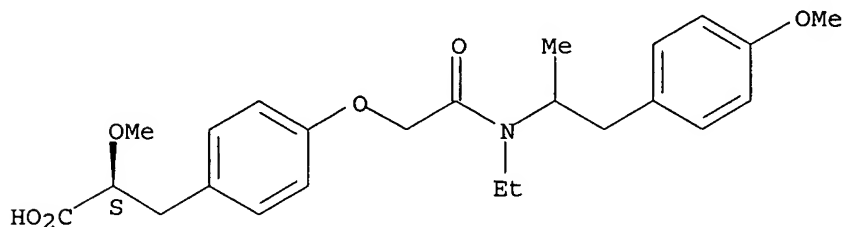
Absolute stereochemistry.



RN 638189-90-9 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[ethyl[2-(4-methoxyphenyl)-1-methylethyl]amino]-2-oxoethoxy]- $\alpha$ -methoxy-, ( $\alpha$ S)-(9CI) (CA INDEX NAME)

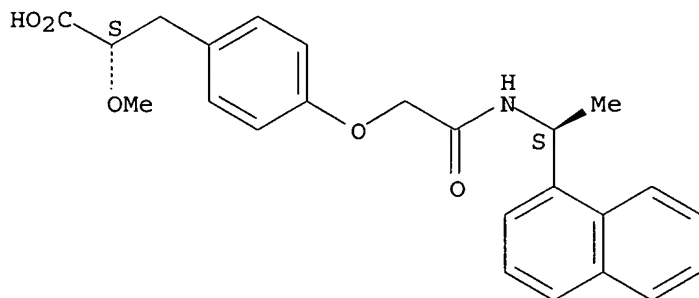
Absolute stereochemistry.



RN 638189-91-0 HCAPLUS

CN Benzenepropanoic acid,  $\alpha$ -methoxy-4-[2-[[1S]-1-(1-naphthalenyl)ethyl]amino]-2-oxoethoxy]-, ( $\alpha$ S)-(9CI) (CA INDEX NAME)

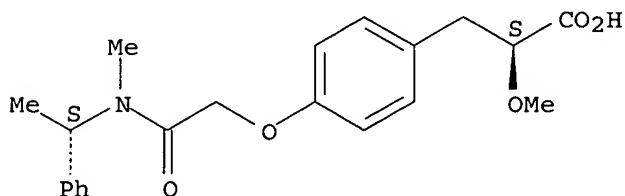
Absolute stereochemistry.



RN 638189-93-2 HCAPLUS

CN Benzenepropanoic acid,  $\alpha$ -methoxy-4-[2-[methyl[1S]-1-phenylethyl]amino]-2-oxoethoxy]-, ( $\alpha$ S)-(9CI) (CA INDEX NAME)

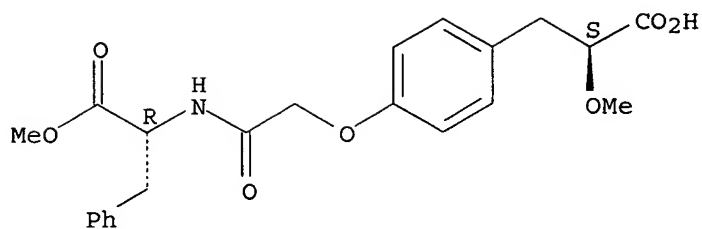
Absolute stereochemistry.



RN 638189-96-5 HCAPLUS

CN D-Phenylalanine, N-[[4-[(2S)-2-carboxy-2-methoxyethyl]phenoxy]acetyl]-,  $\alpha$ -methyl ester (9CI) (CA INDEX NAME)

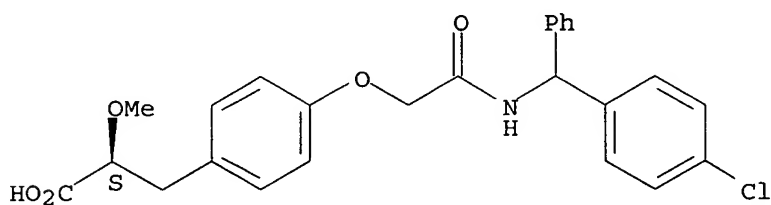
Absolute stereochemistry.



RN 638189-98-7 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[[(4-chlorophenyl)phenylmethyl]amino]-2-oxoethoxy]-α-methoxy-, (αS)- (9CI) (CA INDEX NAME)

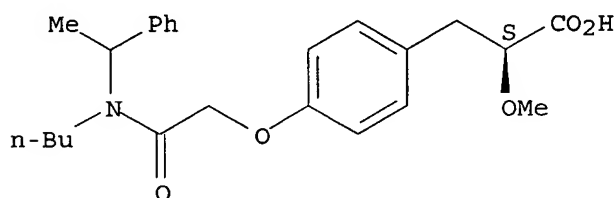
Absolute stereochemistry.



RN 638189-99-8 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[butyl(1-phenylethyl)amino]-2-oxoethoxy]-α-methoxy-, (αS)- (9CI) (CA INDEX NAME)

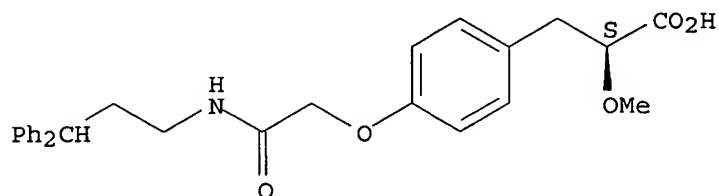
Absolute stereochemistry.



RN 638190-00-8 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[(3,3-diphenylpropyl)amino]-2-oxoethoxy]-α-methoxy-, (αS)- (9CI) (CA INDEX NAME)

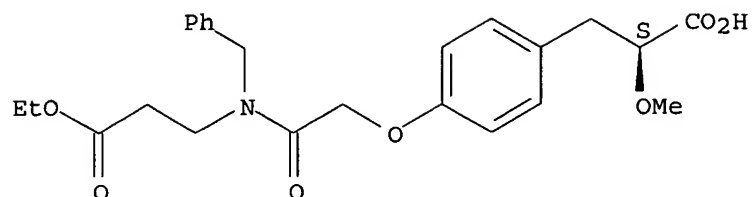
Absolute stereochemistry.



RN 638190-01-9 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[(3-ethoxy-3-oxopropyl)(phenylmethyl)amino]-2-oxoethoxy]-α-methoxy-, (αS)- (9CI) (CA INDEX NAME)

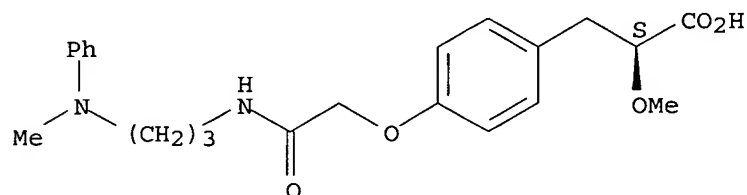
Absolute stereochemistry.



RN 638190-02-0 HCAPLUS

CN Benzenepropanoic acid,  $\alpha$ -methoxy-4-[2-[[3-(methylphenylamino)propyl]amino]-2-oxoethoxy]-, ( $\alpha$ S) - (9CI)  
(CA INDEX NAME)

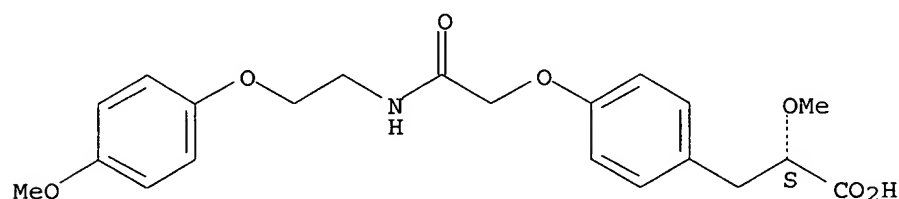
Absolute stereochemistry.



RN 638190-03-1 HCAPLUS

CN Benzenepropanoic acid,  $\alpha$ -methoxy-4-[2-[[2-(4-methoxyphenoxy)ethyl]amino]-2-oxoethoxy]-, ( $\alpha$ S) - (9CI) (CA INDEX NAME)

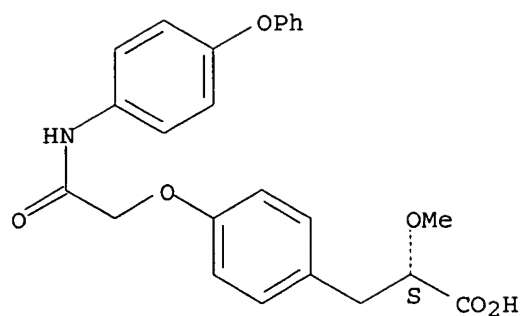
Absolute stereochemistry.



RN 638190-04-2 HCAPLUS

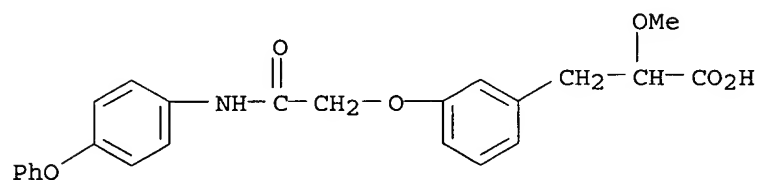
CN Benzenepropanoic acid,  $\alpha$ -methoxy-4-[2-oxo-2-[(4-phenoxyphenyl)amino]ethoxy]-, ( $\alpha$ S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.



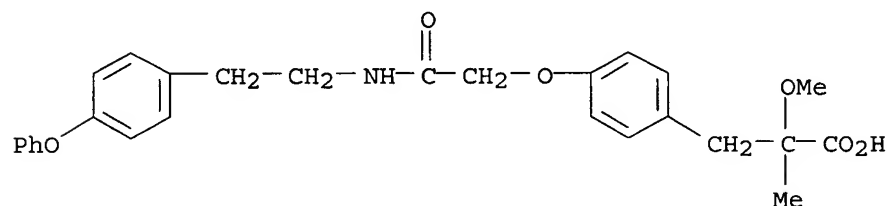
RN 638190-05-3 HCAPLUS

CN Benzenepropanoic acid, α-methoxy-3-[2-oxo-2-[(4-phenoxyphenyl)amino]ethoxy]- (9CI) (CA INDEX NAME)



RN 638190-08-6 HCAPLUS

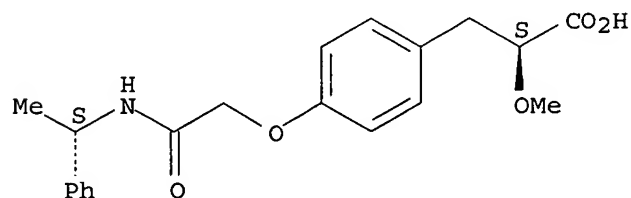
CN Benzenepropanoic acid, α-methoxy-α-methyl-4-[2-oxo-2-[[2-(4-phenoxyphenyl)ethyl]amino]ethoxy]- (9CI) (CA INDEX NAME)



RN 638190-32-6 HCAPLUS

CN Benzenepropanoic acid, α-methoxy-4-[2-oxo-2-[[2-(4-phenoxyphenyl)ethyl]amino]ethoxy]-, (αS)- (9CI) (CA INDEX NAME)

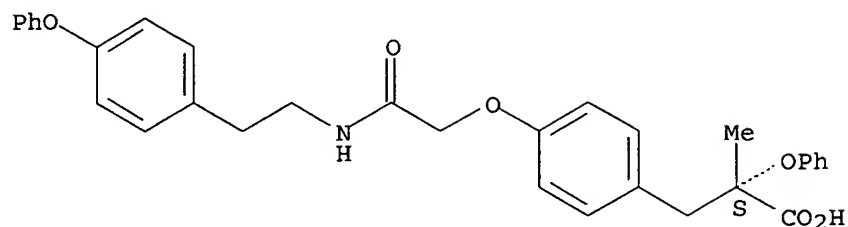
Absolute stereochemistry.



RN 638190-61-1 HCAPLUS

CN Benzenepropanoic acid, α-methyl-4-[2-oxo-2-[[2-(4-phenoxyphenyl)ethyl]amino]ethoxy]-α-phenoxy-, (αS)- (9CI) (CA INDEX NAME)

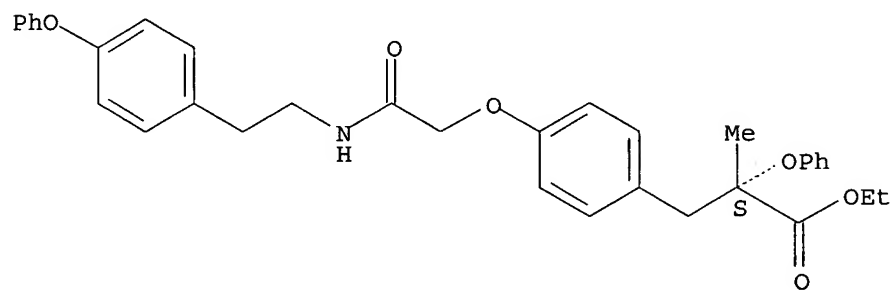
Absolute stereochemistry.



RN 638190-62-2 HCAPLUS

CN Benzenepropanoic acid,  $\alpha$ -methyl-4-[2-oxo-2-[[2-(4-phenoxyphenyl)ethyl]amino]ethoxy]- $\alpha$ -phenoxy-, ethyl ester, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

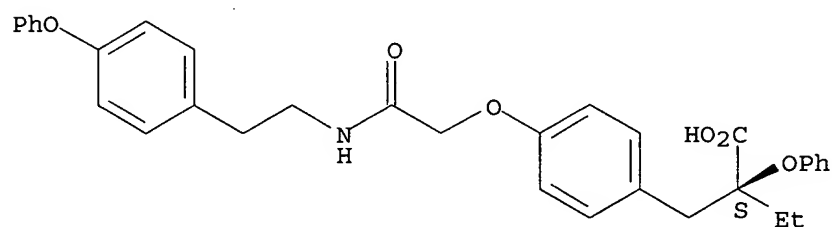
Absolute stereochemistry.



RN 638190-63-3 HCAPLUS

CN Benzenepropanoic acid,  $\alpha$ -ethyl-4-[2-oxo-2-[[2-(4-phenoxyphenyl)ethyl]amino]ethoxy]- $\alpha$ -phenoxy-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 638190-65-5 HCAPLUS

CN Benzenepropanoic acid,  $\alpha$ -methyl-4-[2-oxo-2-[[2-(4-phenoxyphenyl)ethyl]amino]ethoxy]- $\alpha$ -[4-(trifluoromethoxy)phenoxy]-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



Benzenepropanoic acid,  $\alpha$ -(4-fluorophenoxy)- $\alpha$ -methyl-4-[2-oxo-2-[2-(4-phenoxyphenyl)ethyl]amino]ethoxy]-, ( $\alpha$ S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



CN Benzenepropanoic acid, 4-[2-[[[1,1'-biphenyl]-4-ylmethyl)amino]-2-oxoethoxy]- $\alpha$ -methoxy-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

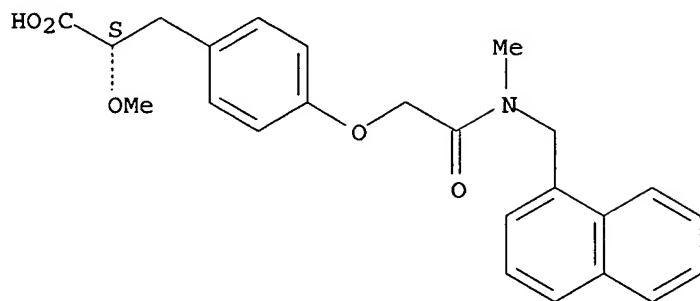
Absolute stereochemistry.



CN	Benzenepropanoic acid, $\alpha$ -methoxy-4-[2-[methyl(1-naphthalenylmethyl)amino]-2-oxoethoxy]-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)
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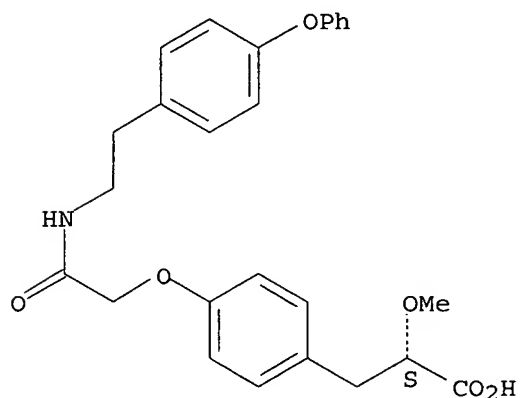
Absolute stereochemistry.



RN 638190-73-5 HCAPLUS

CN Benzenepropanoic acid, α-methoxy-4-[2-oxo-2-[[2-(4-phenoxyphenyl)ethyl]amino]ethoxy]-, (αS)- (9CI) (CA INDEX NAME)

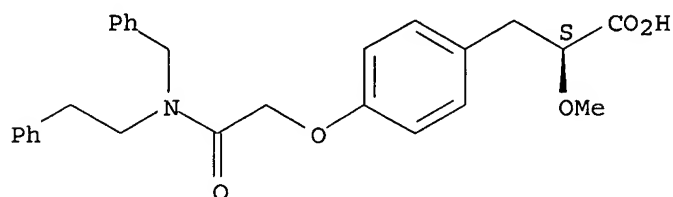
Absolute stereochemistry.



RN 638190-75-7 HCAPLUS

CN Benzenepropanoic acid, α-methoxy-4-[2-oxo-2-[(2-phenylethyl)(phenylmethyl)amino]ethoxy]-, (αS)- (9CI) (CA INDEX NAME)

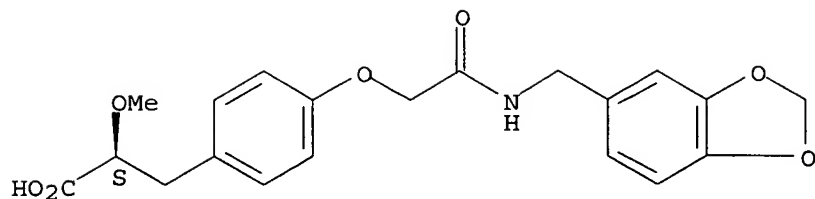
Absolute stereochemistry.



RN 638190-81-5 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[(1,3-benzodioxol-5-ylmethyl)amino]-2-oxoethoxy]-α-methoxy-, (αS)- (9CI) (CA INDEX NAME)

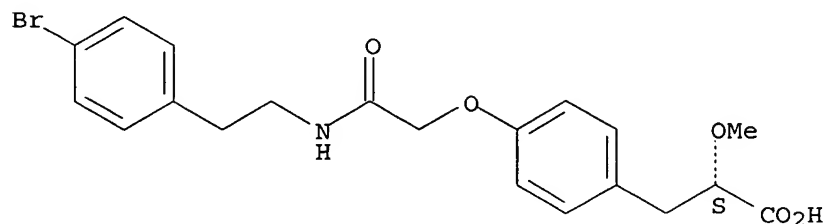
Absolute stereochemistry.



RN 638190-82-6 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[2-(4-bromophenyl)ethyl]amino]-2-oxoethoxy]-α-methoxy-, (αS)- (9CI) (CA INDEX NAME)

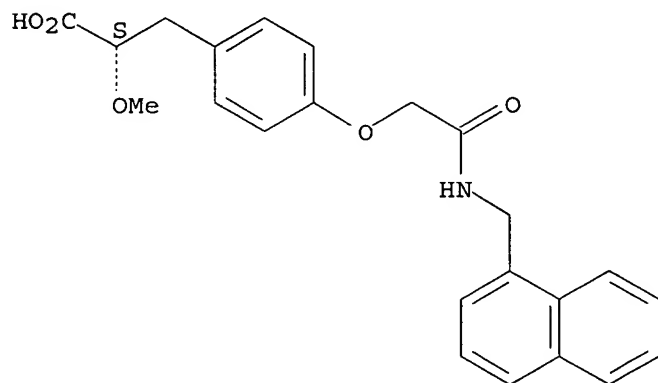
Absolute stereochemistry.



RN 638190-83-7 HCAPLUS

CN Benzenepropanoic acid, α-methoxy-4-[2-[(1-naphthalenylmethyl)amino]-2-oxoethoxy]-, (αS)- (9CI) (CA INDEX NAME)

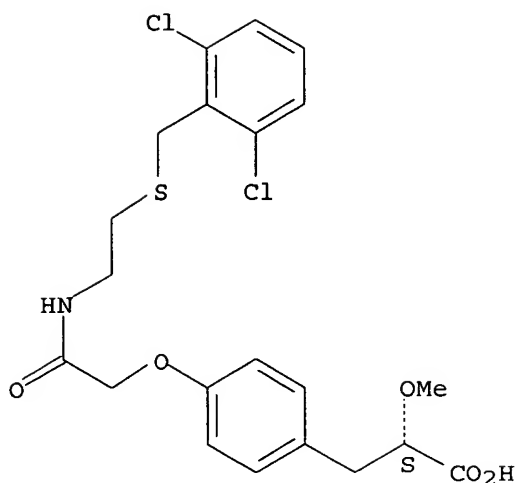
Absolute stereochemistry.



RN 638190-84-8 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[2-[[2-(2,6-dichlorophenyl)methyl]thio]ethyl]amino]-2-oxoethoxy]-α-methoxy-, (αS)- (9CI) (CA INDEX NAME)

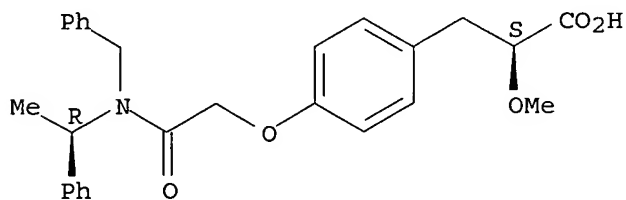
Absolute stereochemistry.



RN 638190-85-9 HCAPLUS

CN Benzenepropanoic acid, α-methoxy-4-[2-oxo-2-[[1R]-1-phenylethyl](phenylmethyl)amino]ethoxy-, (αS)- (9CI) (CA INDEX NAME)

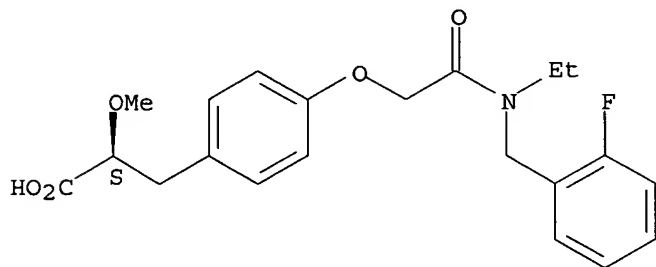
Absolute stereochemistry.



RN 638190-88-2 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[ethyl[(2-fluorophenyl)methyl]amino]-2-oxoethoxy]-α-methoxy-, (αS)- (9CI) (CA INDEX NAME)

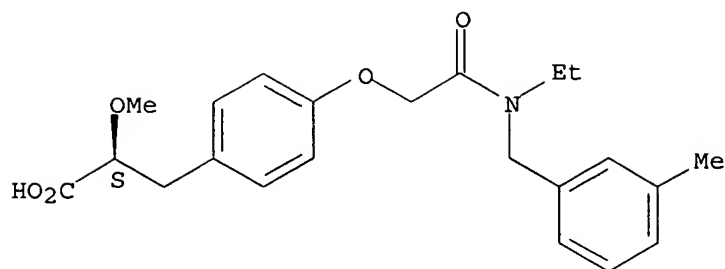
Absolute stereochemistry.



RN 638190-89-3 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[ethyl[(3-methylphenyl)methyl]amino]-2-oxoethoxy]-α-methoxy-, (αS)- (9CI) (CA INDEX NAME)

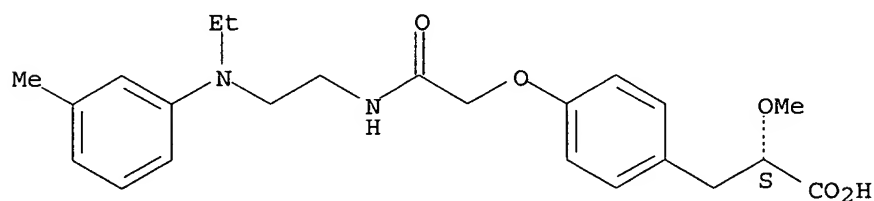
Absolute stereochemistry.



RN 638190-92-8 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[2-[ethyl(3-methylphenyl)amino]ethyl]amino]-2-oxoethoxy]-α-methoxy-, (αS)- (9CI) (CA INDEX NAME)

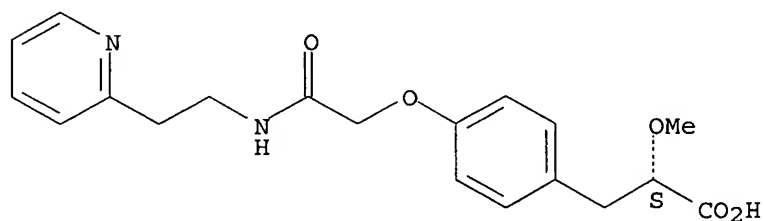
Absolute stereochemistry.



RN 638190-93-9 HCAPLUS

CN Benzenepropanoic acid, α-methoxy-4-[2-oxo-2-[[2-(2-pyridinyl)ethyl]amino]ethoxy]-, (αS)- (9CI) (CA INDEX NAME)

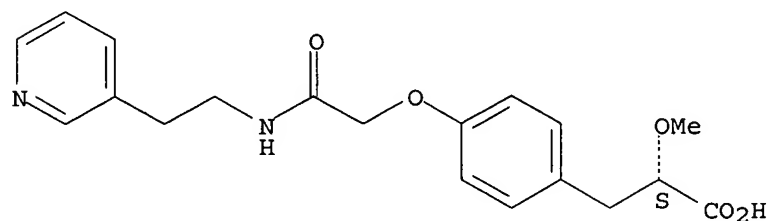
Absolute stereochemistry.



RN 638190-94-0 HCAPLUS

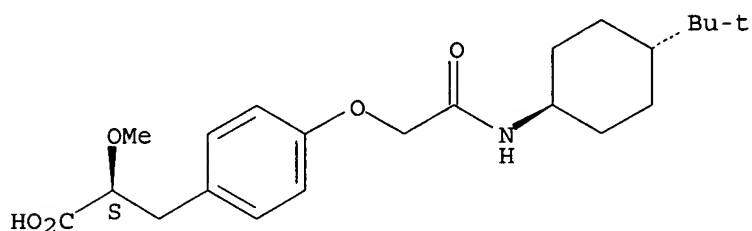
CN Benzenepropanoic acid, α-methoxy-4-[2-oxo-2-[[2-(3-pyridinyl)ethyl]amino]ethoxy]-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



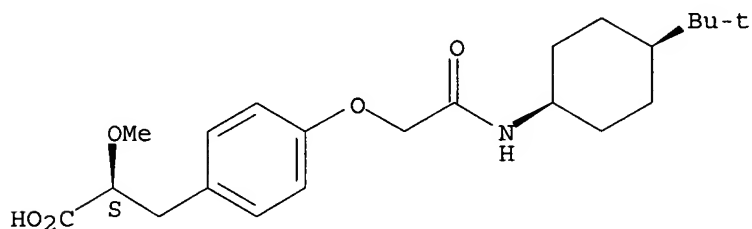
RN 638190-95-1 HCAPLUS  
 CN Benzenepropanoic acid, 4-[2-[[trans-4-(1,1-dimethylethyl)cyclohexyl]amino]-2-oxoethoxy]- $\alpha$ -methoxy-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



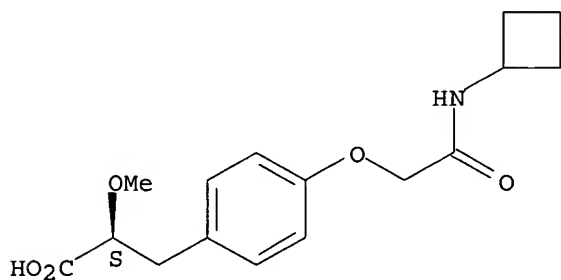
RN 638190-96-2 HCAPLUS  
 CN Benzenepropanoic acid, 4-[2-[[cis-4-(1,1-dimethylethyl)cyclohexyl]amino]-2-oxoethoxy]- $\alpha$ -methoxy-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



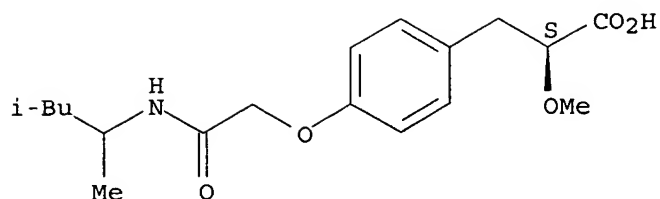
RN 638190-97-3 HCAPLUS  
 CN Benzenepropanoic acid, 4-[2-(cyclobutylamino)-2-oxoethoxy]- $\alpha$ -methoxy-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 638190-98-4 HCAPLUS  
 CN Benzenepropanoic acid, 4-[2-[(1,3-dimethylbutyl)amino]-2-oxoethoxy]- $\alpha$ -methoxy-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

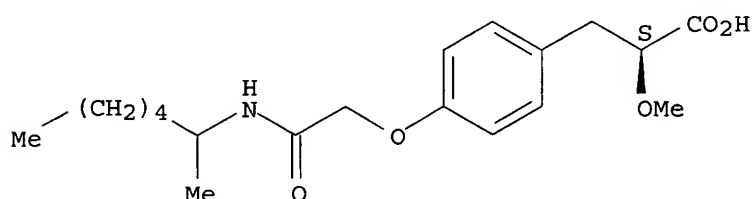
Absolute stereochemistry.



RN 638190-99-5 HCAPLUS

CN Benzenepropanoic acid, α-methoxy-4-[2-[(1-methylhexyl)amino]-2-oxoethoxy]-, (αS)- (9CI) (CA INDEX NAME)

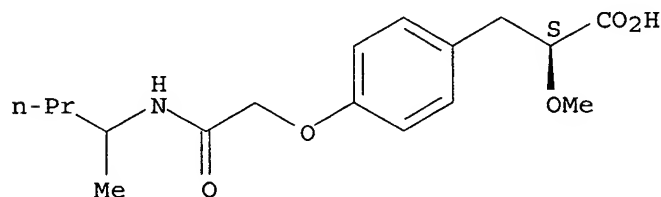
Absolute stereochemistry.



RN 638191-00-1 HCAPLUS

CN Benzenepropanoic acid, α-methoxy-4-[2-[(1-methylbutyl)amino]-2-oxoethoxy]-, (αS)- (9CI) (CA INDEX NAME)

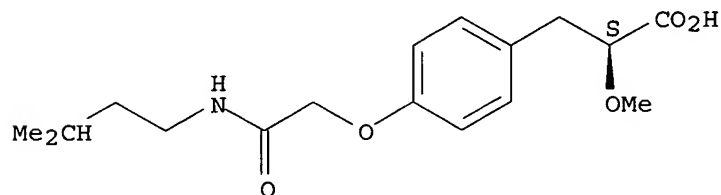
Absolute stereochemistry.



RN 638191-01-2 HCAPLUS

CN Benzenepropanoic acid, α-methoxy-4-[2-[(3-methylbutyl)amino]-2-oxoethoxy]-, (αS)- (9CI) (CA INDEX NAME)

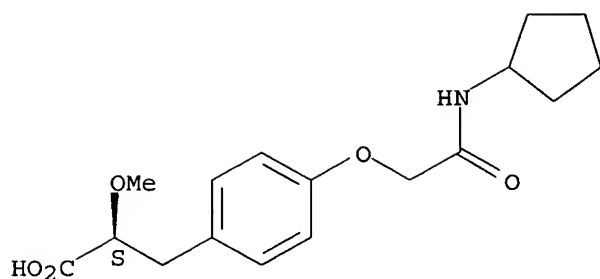
Absolute stereochemistry.



RN 638191-02-3 HCAPLUS

CN Benzenepropanoic acid, 4-[2-(cyclopentylamino)-2-oxoethoxy]-α-methoxy-, (αS)- (9CI) (CA INDEX NAME)

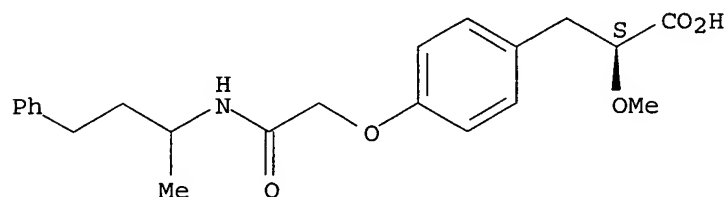
Absolute stereochemistry.



RN 638191-03-4 HCAPLUS

CN Benzenepropanoic acid, α-methoxy-4-[2-[(1-methyl-3-phenylpropyl)amino]-2-oxoethoxy]-, (αS)- (9CI) (CA INDEX NAME)

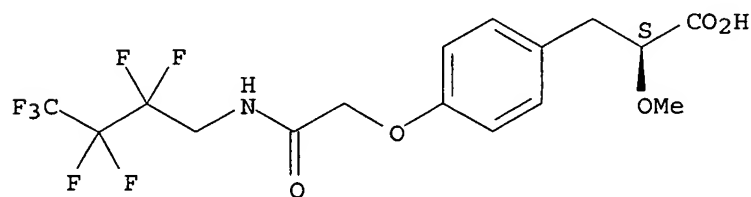
Absolute stereochemistry.



RN 638191-04-5 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[(2,2,3,3,4,4,4-heptafluorobutyl)amino]-2-oxoethoxy]-α-methoxy-, (αS)- (9CI) (CA INDEX NAME)

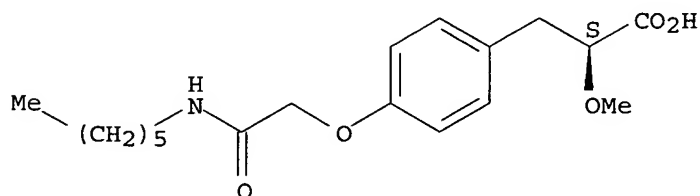
Absolute stereochemistry.



RN 638191-08-9 HCAPLUS

CN Benzenepropanoic acid, 4-[2-(hexylamino)-2-oxoethoxy]-α-methoxy-, (αS)- (9CI) (CA INDEX NAME)

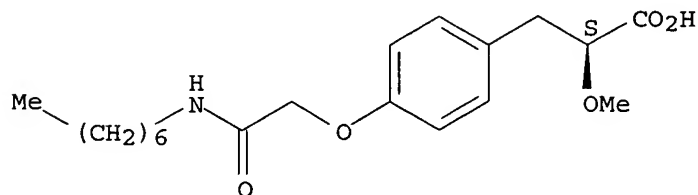
Absolute stereochemistry.



RN 638191-09-0 HCAPLUS

CN Benzenepropanoic acid, 4-[2-(heptylamino)-2-oxoethoxy]- $\alpha$ -methoxy-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

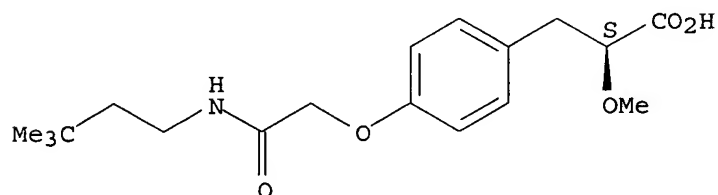
Absolute stereochemistry.



RN 638191-10-3 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[(3,3-dimethylbutyl)amino]-2-oxoethoxy]- $\alpha$ -methoxy-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

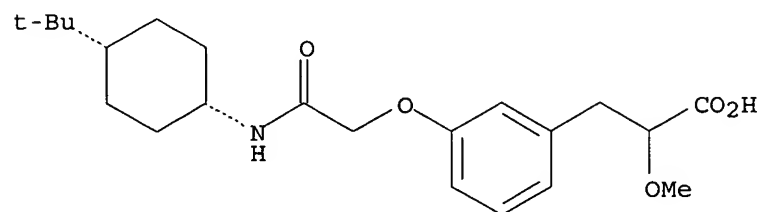
Absolute stereochemistry.



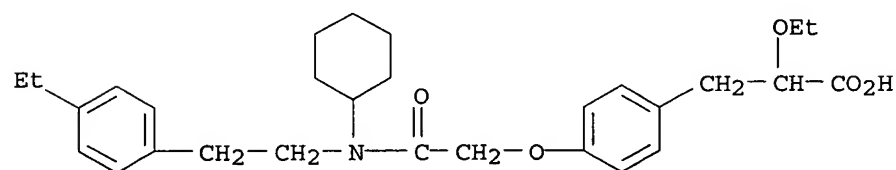
RN 638191-11-4 HCAPLUS

CN Benzenepropanoic acid, 3-[2-[[cis-4-(1,1-dimethylethyl)cyclohexyl]amino]-2-oxoethoxy]- $\alpha$ -methoxy- (9CI) (CA INDEX NAME)

Relative stereochemistry.



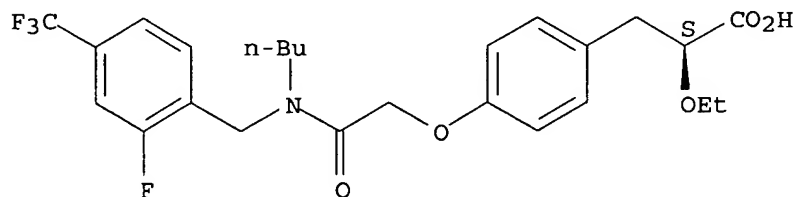
RN 638191-24-9 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[cyclohexyl[2-(4-ethylphenyl)ethyl]amino]-2-oxoethoxy]- $\alpha$ -ethoxy- (9CI) (CA INDEX NAME)



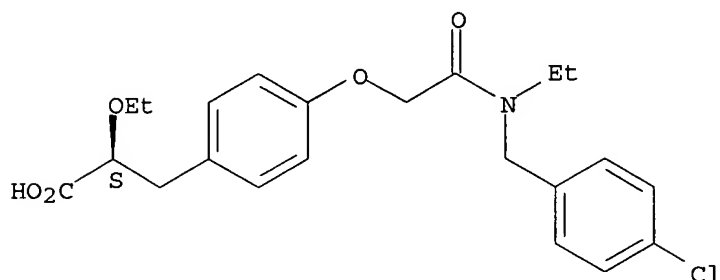
RN 719277-13-1 HCAPLUS  
 CN Benzenepropanoic acid, 4-[2-[butyl[[2-fluoro-4-(trifluoromethyl)phenyl]methyl]amino]-2-oxoethoxy]- $\alpha$ -ethoxy-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



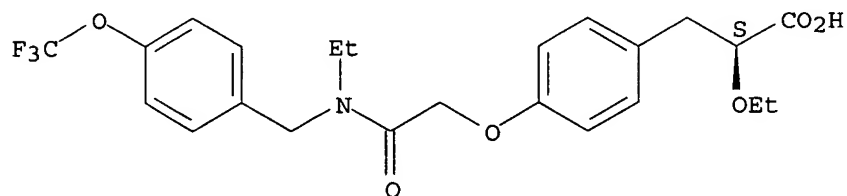
RN 719277-14-2 HCAPLUS  
 CN Benzenepropanoic acid, 4-[2-[[[4-chlorophenyl]methyl]ethylamino]-2-oxoethoxy]- $\alpha$ -ethoxy-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



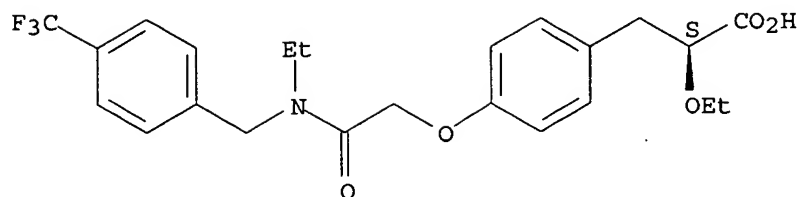
RN 719277-15-3 HCAPLUS  
 CN Benzenepropanoic acid,  $\alpha$ -ethoxy-4-[2-[ethyl[[4-(trifluoromethoxy)phenyl]methyl]amino]-2-oxoethoxy]-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 719277-16-4 HCAPLUS  
 CN Benzenepropanoic acid,  $\alpha$ -ethoxy-4-[2-[ethyl[[4-(trifluoromethyl)phenyl]methyl]amino]-2-oxoethoxy]-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

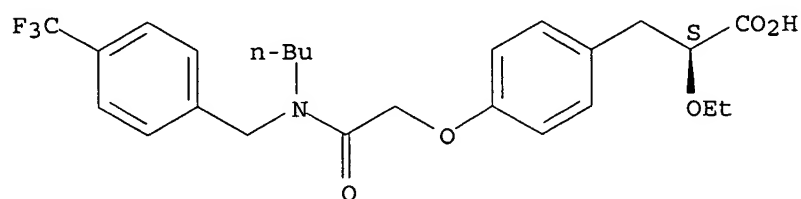
Absolute stereochemistry.



RN 719277-17-5 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[butyl[[4-(trifluoromethyl)phenyl]methyl]amino]-2-oxoethoxy]-α-ethoxy-, (αS)- (9CI) (CA INDEX NAME)

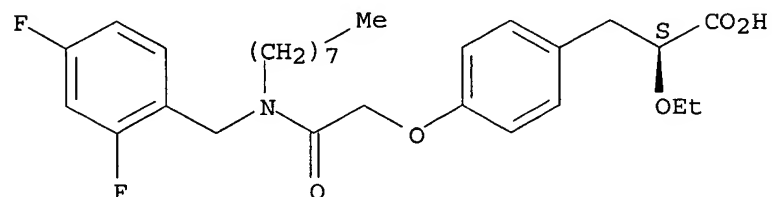
Absolute stereochemistry.



RN 816465-03-9 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[2,4-difluorophenyl]methyl]octylamino]-2-oxoethoxy]-α-ethoxy-, (αS)- (9CI) (CA INDEX NAME)

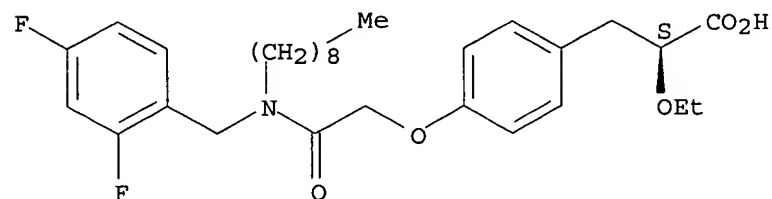
Absolute stereochemistry.



RN 816465-07-3 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[2,4-difluorophenyl]methyl]nonylamino]-2-oxoethoxy]-α-ethoxy-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

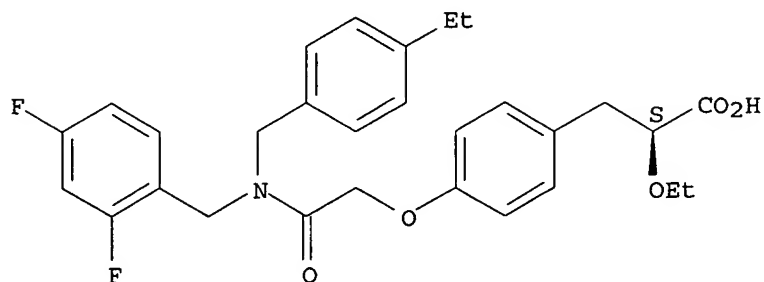


RN 816465-11-9 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[2,4-difluorophenyl]methyl]-(4-

ethylphenyl)methyl] amino]-2-oxoethoxy]- $\alpha$ -ethoxy-,  
( $\alpha$ S)- (9CI) (CA INDEX NAME)

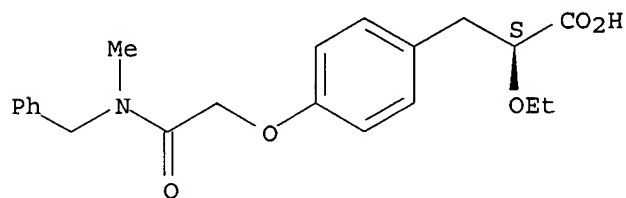
Absolute stereochemistry.



RN 816465-15-3 HCAPLUS

CN Benzenepropanoic acid,  $\alpha$ -ethoxy-4-[2-[methyl(phenylmethyl)amino]-2-oxoethoxy]-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

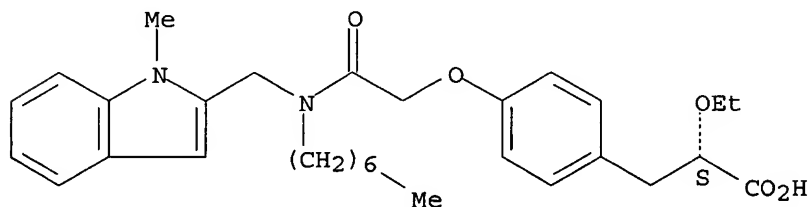
Absolute stereochemistry.



RN 816465-17-5 HCAPLUS

CN Benzenepropanoic acid,  $\alpha$ -ethoxy-4-[2-[heptyl[(1-methyl-1H-indol-2-yl)methyl]amino]-2-oxoethoxy]-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

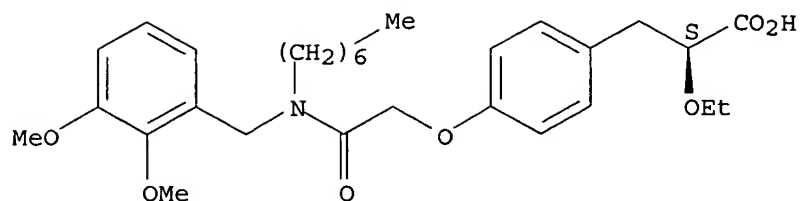
Absolute stereochemistry.



RN 816465-20-0 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[2,3-dimethoxyphenyl)methyl]heptylamino]-2-oxoethoxy]- $\alpha$ -ethoxy-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

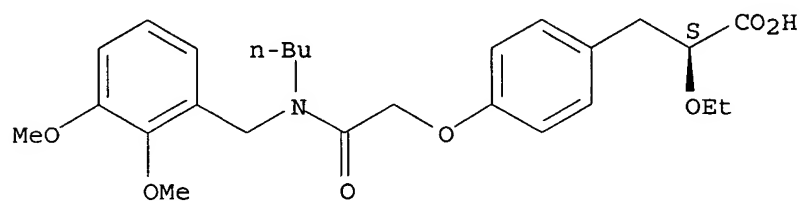
Absolute stereochemistry.



RN 816465-23-3 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[butyl[(2,3-dimethoxyphenyl)methyl]amino]-2-oxoethoxy]- $\alpha$ -ethoxy-, ( $\alpha$ S) - (9CI) (CA INDEX NAME)

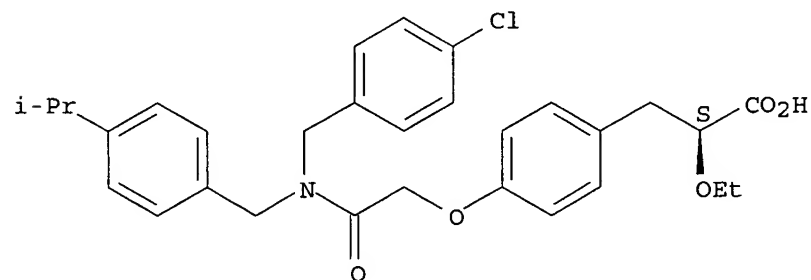
Absolute stereochemistry.



RN 816465-25-5 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[[4-chlorophenyl)methyl][4-(1-methylethyl)phenyl)methyl]amino]-2-oxoethoxy]- $\alpha$ -ethoxy-, ( $\alpha$ S) - (9CI) (CA INDEX NAME)

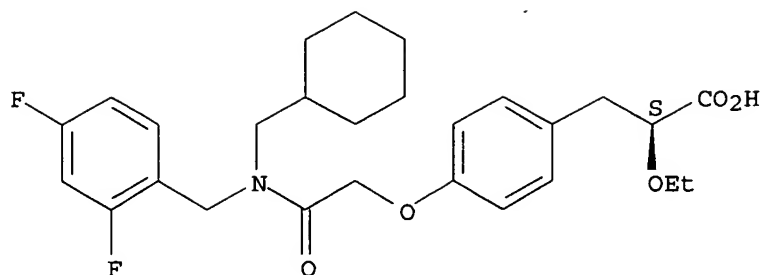
Absolute stereochemistry.



RN 816465-28-8 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[(cyclohexylmethyl)[(2,4-difluorophenyl)methyl]amino]-2-oxoethoxy]- $\alpha$ -ethoxy-, ( $\alpha$ S) - (9CI) (CA INDEX NAME)

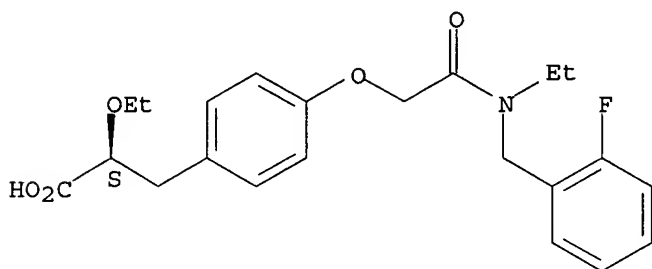
Absolute stereochemistry.



RN 816465-33-5 HCAPLUS

CN Benzenepropanoic acid,  $\alpha$ -ethoxy-4-[2-[ethyl[(2-fluorophenyl)methyl]amino]-2-oxoethoxy]-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

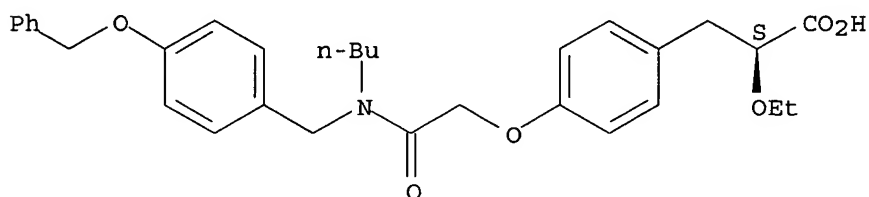
Absolute stereochemistry.



RN 816465-35-7 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[butyl[[4-(phenylmethoxy)phenyl]methyl]amino]-2-oxoethoxy]- $\alpha$ -ethoxy-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

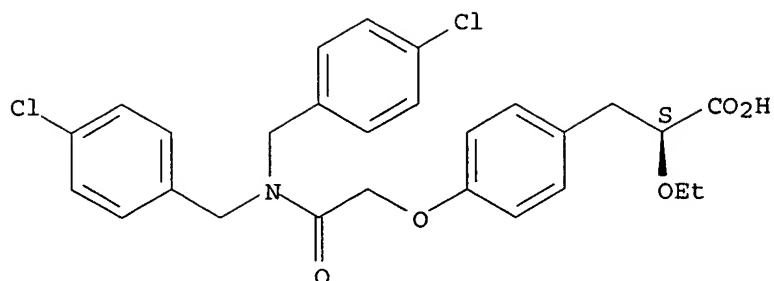
Absolute stereochemistry.



RN 816465-37-9 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[bis[(4-chlorophenyl)methyl]amino]-2-oxoethoxy]- $\alpha$ -ethoxy-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

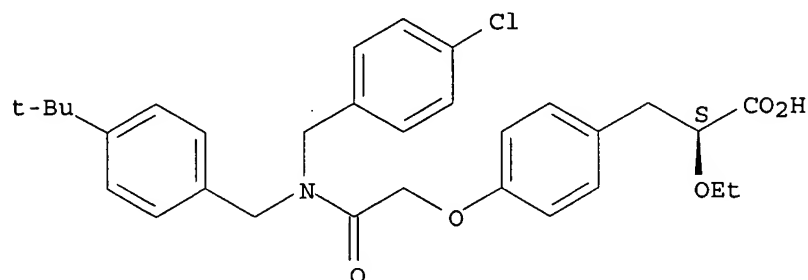
Absolute stereochemistry.



RN 816465-43-7 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[[4-chlorophenyl)methyl][[4-(1,1-dimethylethyl)phenyl)methyl]amino]-2-oxoethoxy]-α-ethoxy-, (αS) - (9CI) (CA INDEX NAME)

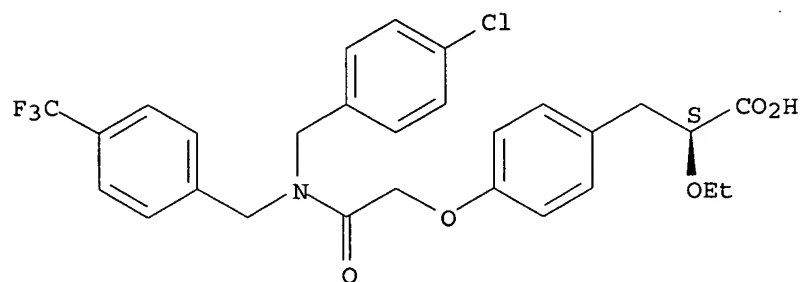
Absolute stereochemistry.



RN 816465-47-1 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[[4-chlorophenyl)methyl][[4-(trifluoromethyl)phenyl)methyl]amino]-2-oxoethoxy]-α-ethoxy-, (αS) - (9CI) (CA INDEX NAME)

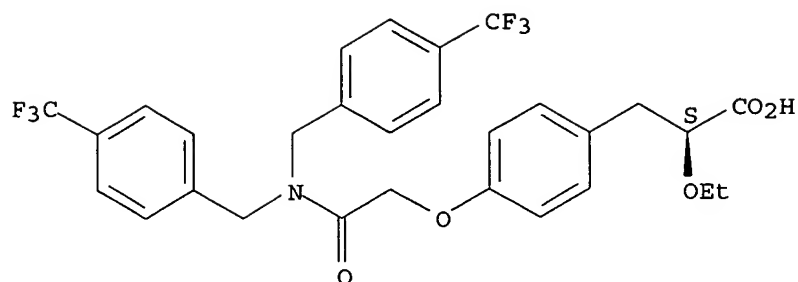
Absolute stereochemistry.



RN 816465-51-7 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[bis[[4-(trifluoromethyl)phenyl)methyl]amino]-2-oxoethoxy]-α-ethoxy-, (αS) - (9CI) (CA INDEX NAME)

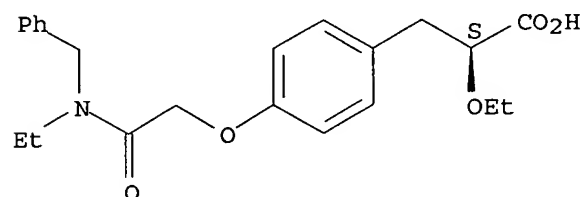
Absolute stereochemistry.



RN 816465-55-1 HCAPLUS

CN Benzenepropanoic acid, α-ethoxy-4-[2-[ethyl(phenylmethyl)amino]-2-oxoethoxy]-, (αS)- (9CI) (CA INDEX NAME)

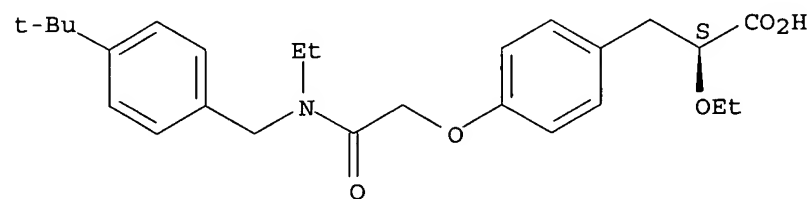
Absolute stereochemistry.



RN 816465-57-3 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[[4-(1,1-dimethylethyl)phenyl]methyl]ethylamino]-2-oxoethoxy]-α-ethoxy-, (αS)- (9CI) (CA INDEX NAME)

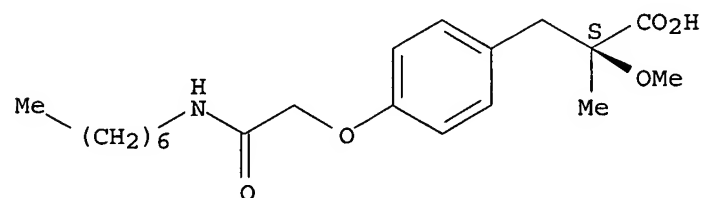
Absolute stereochemistry.



RN 816465-64-2 HCAPLUS

CN Benzenepropanoic acid, 4-[2-(heptylamino)-2-oxoethoxy]-α-methoxy-α-methyl-, (αS)- (9CI) (CA INDEX NAME)

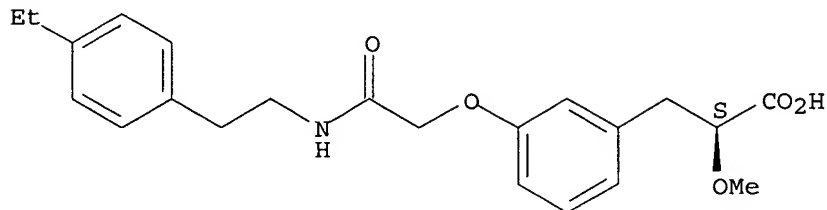
Absolute stereochemistry.



RN 816465-67-5 HCAPLUS

CN Benzenepropanoic acid, 3-[2-[[2-(4-ethylphenyl)ethyl]amino]-2-oxoethoxy]- $\alpha$ -methoxy-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

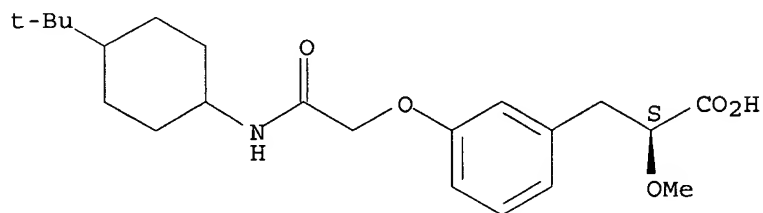
Absolute stereochemistry.



RN 817181-62-7 HCAPLUS

CN Benzenepropanoic acid, 3-[2-[[4-(1,1-dimethylethyl)cyclohexyl]amino]-2-oxoethoxy]- $\alpha$ -methoxy-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

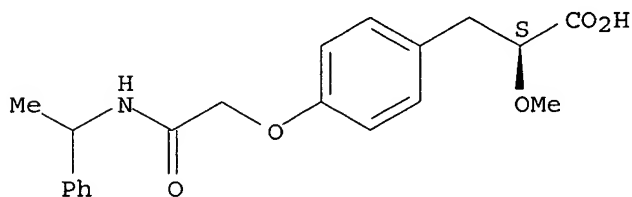
Absolute stereochemistry.



RN 871731-30-5 HCAPLUS

CN Benzenepropanoic acid,  $\alpha$ -methoxy-4-[2-oxo-2-[(1-phenylethyl)amino]ethoxy]-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IC ICM A61K031-496

ICS A61K049-04; A61K031-44; A61K031-195

INCL 514255030; 514357000; 514567000; 544392000; 546335000; 562442000

CC 25-19 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)

Section cross-reference(s): 1, 27, 28

ST phenylalkanamide phenoxyalkanamide prepn modulator

**peroxisome** proliferator activated receptor;

phenoxyacetamide prepn modulator **peroxisome** proliferator

activated receptor; lipid disorder dyslipidemias metabolic

syndrome treatment phenoxyacetamide prepn

IT Metabolic disorders



(metabolic syndrome X; preparation of phenoxyacetamide derivs. as modulators of **peroxisome** proliferator-activated receptors for treating metabolic disorder)

IT Human

(preparation of phenoxyacetamide derivs. as modulators of **peroxisome** proliferator-activated receptors for treating metabolic disorder)

IT Dyslipidemia

**Peroxisome** proliferator-activated receptors

(preparation of phenoxyacetamide derivs. as modulators of **peroxisome** proliferator-activated receptors for treating metabolic disorder)

IT **Peroxisome** proliferator-activated receptors

( $\alpha$ ; preparation of phenoxyacetamide derivs. as modulators of **peroxisome** proliferator-activated receptors for treating metabolic disorder)

IT 114413-73-9P, N-Butyl-N-(2,3-dimethoxybenzyl)amine 500789-57-1P, N-Butyl-2,3-dimethoxybenzamide 549501-67-9P, Ethyl (2S)-3-[4-[2-(benzyloxy)-2-oxoethoxy]phenyl]-2-ethoxypropanoate 549501-68-0P, [4-((2S)-2,3-Diethoxy-3-oxopropyl)phenoxy]acetic acid 549501-69-1P, N-(Cyclohexylmethyl)heptanamide 549501-70-4P, N-(Cyclohexylmethyl)-N-heptylamine hydrochloride 549501-71-5P, Ethyl (2S)-3-[4-[2-[(cyclohexylmethyl)(heptyl)amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoate 549501-73-7P, N-(2,4-Difluorobenzyl)heptanamide 549501-74-8P, N-(2,4-Difluorobenzyl)heptylamine hydrochloride 549501-75-9P, Ethyl (2S)-3-[4-[2-[(2,4-difluorobenzyl)(heptyl)amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoate 549532-34-5P, Ethyl (2S)-3-[4-[2-[benzyl(hexyl)amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoate 549532-36-7P, Ethyl (2S)-2-ethoxy-3-[4-[2-[hexyl(2-phenylethyl)amino]-2-oxoethoxy]phenyl]propanoate 637015-19-1P, N-(2,3-Dimethoxybenzyl)-N-heptylamine 719277-18-6P, N-Butyl-N-[2-fluoro-4-(trifluoromethyl)benzyl]amine 719277-19-7P, Ethyl (2S)-3-[4-[2-[butyl[2-fluoro-4-(trifluoromethyl)benzyl]amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoate 719277-20-0P, Ethyl (2S)-3-[4-[2-[(4-chlorobenzyl)(ethyl)amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoate 719277-21-1P, N-[4-(Trifluoromethoxy)benzyl]acetamide 719277-22-2P, N-Ethyl-N-[4-(Trifluoromethoxy)benzyl]amine 719277-23-3P, 719277-24-4P, Ethyl (2S)-2-ethoxy-3-[4-[2-[ethyl[4-(trifluoromethyl)benzyl]amino]-2-oxoethoxy]phenyl]propanoate 765303-27-3P, Ethyl (2S)-3-[4-[2-[butyl[4-(trifluoromethyl)benzyl]amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoate 816465-04-0P, N-(2,4-Difluorobenzyl)octanamide 816465-05-1P, N-(2,4-Difluorobenzyl)octylamine hydrochloride 816465-06-2P, Ethyl (2S)-3-[4-[2-[(2,4-difluorobenzyl)(octyl)amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoate 816465-08-4P, N-(2,4-Difluorobenzyl)nonanamide 816465-09-5P, N-(2,4-Difluorobenzyl)nonylamine hydrochloride 816465-10-8P, Ethyl (2S)-3-[4-[2-[(2,4-difluorobenzyl)(nonyl)amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoate 816465-12-0P, N-(2,4-Difluorobenzyl)-4-ethylbenzamide 816465-13-1P, N-(2,4-Difluorobenzyl)-N-(4-ethylbenzyl)amine 816465-14-2P, Ethyl (2S)-3-[4-[2-[(2,4-difluorobenzyl)(4-ethylbenzyl)amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoate 816465-16-4P, Ethyl (2S)-3-[4-[2-[benzyl(methyl)amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoate 816465-18-6P, N-Heptyl-N-[(1-methylindol-2-yl)methyl]amine 816465-19-7P, Ethyl (2S)-2-ethoxy-3-[4-[2-[heptyl[(1-methylindol-2-yl)methyl]amino]-2-oxoethoxy]phenyl]propanoate 816465-21-1P,

N-Heptyl-2,3-dimethoxybenzamide 816465-22-2P, Ethyl (2S)-3-[4-[2-[(2,3-dimethoxybenzyl)(heptyl)amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoate 816465-24-4P, Ethyl (2S)-3-[4-[2-[butyl(2,3-dimethoxybenzyl)amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoate 816465-26-6P, N-(4-Chlorobenzyl)-N-(4-isopropylbenzyl)amine 816465-27-7P, Ethyl (2S)-3-[4-[2-[(4-chlorobenzyl)(4-isopropylbenzyl)amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoate 816465-29-9P, N-(Cyclohexylmethyl)-N-(2,4-difluorobenzyl)amine 816465-31-3P, Ethyl (2S)-3-[4-[2-[(cyclohexylmethyl)(2,4-difluorobenzyl)amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoate 816465-34-6P, Ethyl (2S)-2-ethoxy-3-[4-[2-[ethyl(2-fluorobenzyl)amino]-2-oxoethoxy]phenyl]propanoate 816465-36-8P, Ethyl (2S)-3-[4-[2-[[4-(benzyloxy)benzyl](butyl)amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoate 816465-39-1P, Ethyl (2S)-3-[4-[2-[bis(4-chlorobenzyl)amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoate 816465-45-9P, N-(4-tert-Butylbenzyl)-N-(4-chlorobenzyl)amine 816465-46-0P, Ethyl (2S)-3-[4-[2-[(4-tert-butylbenzyl)(4-chlorobenzyl)amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoate 816465-49-3P, Ethyl (2S)-3-[4-[2-[(4-chlorobenzyl)(4-(trifluoromethyl)benzyl)amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoate 816465-52-8P, Ethyl (2S)-3-[4-[2-[bis(4-(trifluoromethyl)benzyl)amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoate 816465-56-2P, Ethyl (2S)-3-[4-[2-[benzyl(ethyl)amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoate 816465-58-4P, Ethyl (2S)-3-[4-[2-[(4-tert-butylbenzyl)(ethyl)amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoate (intermediate; preparation of phenoxyacetamide derivs. as modulators of peroxisome proliferator-activated receptors for treating metabolic disorder)

IT 549501-66-8P, (2S)-3-[4-[2-[(Cyclohexylmethyl)(heptyl)amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoic acid 549501-72-6P, (2S)-3-[4-[2-[(2,4-Difluorobenzyl)(heptyl)amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoic acid 549532-33-4P, (2S)-3-[4-[2-[Benzyl(hexyl)amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoic acid 549532-35-6P, (2S)-2-Ethoxy-3-[4-[2-[hexyl(2-phenylethyl)amino]-2-oxoethoxy]phenyl]propanoic acid 638189-57-8P 638189-90-9P 638189-91-0P 638189-93-2P 638189-94-3P, (2S)-4-[2-[4-(4-Fluorobenzoyl)-1-piperidinyl]-2-oxoethoxy]- $\alpha$ -methoxybenzenepropanoic acid 638189-95-4P, (2S)-4-[2-[4-(4-Chlorobenzoyl)-1-piperidinyl]-2-oxoethoxy]- $\alpha$ -methoxybenzenepropanoic acid 638189-96-5P 638189-97-6P 638189-98-7P 638189-99-8P 638190-00-8P, (2S)-4-[2-[(3,3-Diphenylpropyl)amino]-2-oxoethoxy]- $\alpha$ -methoxybenzenepropanoic acid 638190-01-9P, (2S)-4-[2-[(3-Ethoxy-3-oxopropyl)(phenylmethyl)amino]-2-oxoethoxy]- $\alpha$ -methoxybenzenepropanoic acid 638190-02-0P 638190-03-1P, (2S)- $\alpha$ -Methoxy-4-[2-[[2-(4-methoxyphenoxy)ethyl]amino]-2-oxoethoxy]benzenepropanoic acid 638190-04-2P 638190-05-3P 638190-08-6P 638190-32-6P 638190-61-1P 638190-62-2P 638190-63-3P 638190-65-5P 638190-67-7P 638190-69-9P, (2S)-4-[2-[[1,1'-Biphenyl-4-yl)methyl]amino]-2-oxoethoxy]- $\alpha$ -methoxybenzenepropanoic acid 638190-70-2P, (2S)- $\alpha$ -Methoxy-4-[2-[methyl[(1-naphthalenyl)methyl]amino]-2-oxoethoxy]benzenepropanoic acid 638190-71-3P, (2S)-4-[2-[4-(Diphenylmethyl)-1-piperazinyl]-2-oxoethoxy]- $\alpha$ -methoxybenzenepropanoic acid 638190-72-4P, (2S)-4-[2-[4-[Bis(4-fluorophenyl)methyl]-1-piperazinyl]-2-oxoethoxy]- $\alpha$ -methoxybenzenepropanoic acid

638190-73-5P 638190-74-6P, (2S)-4-[2-(3,4-Dihydro-2(1H)-isoquinolinyl)-2-oxoethoxy]- $\alpha$ -methoxybenzenepropanoic acid  
638190-75-7P 638190-76-8P, (2S)-4-[2-[4-(4-Fluorophenyl)-1-piperazinyl]-2-oxoethoxy]- $\alpha$ -methoxybenzenepropanoic acid  
638190-77-9P 638190-78-0P, (2S)-4-[2-[4-(3-Chlorophenyl)-1-piperazinyl]-2-oxoethoxy]- $\alpha$ -methoxybenzenepropanoic acid  
638190-79-1P, (2S)-4-[2-[4-[(4-Chlorophenyl)methyl]-1-piperazinyl]-2-oxoethoxy]- $\alpha$ -methoxybenzenepropanoic acid  
638190-81-5P, (2S)-4-[2-[(1,3-Benzodioxol-5-ylmethyl)amino]-2-oxoethoxy]- $\alpha$ -methoxybenzenepropanoic acid  
638190-82-6P, (2S)-4-[2-[[2-(4-Bromophenyl)ethyl]amino]-2-oxoethoxy]- $\alpha$ -methoxybenzenepropanoic acid  
638190-83-7P, (2S)- $\alpha$ -Methoxy-4-[2-[[1-naphthalenyl)methyl]amino]-2-oxoethoxy]benzenepropanoic acid  
638190-84-8P, (2S)-4-[2-[[2-[(2,6-Dichlorophenyl)methyl]thio]ethyl]amino]-2-oxoethoxy]- $\alpha$ -methoxybenzenepropanoic acid 638190-85-9P  
638190-86-0P, (2S)-4-[2-[4-(4-Acetylphenyl)-1-piperazinyl]-2-oxoethoxy]- $\alpha$ -methoxybenzenepropanoic acid 638190-87-1P  
638190-88-2P, (2S)-4-[2-[Ethyl[(2-fluorophenyl)methyl]amino]-2-oxoethoxy]- $\alpha$ -methoxybenzenepropanoic acid 638190-89-3P,  
(2S)-4-[2-[Ethyl[(3-methylphenyl)methyl]amino]-2-oxoethoxy]- $\alpha$ -methoxybenzenepropanoic acid 638190-90-6P,  
(2S)-4-[2-[4-[(4-Fluorophenyl)methyl]-1-piperazinyl]-2-oxoethoxy]- $\alpha$ -methoxybenzenepropanoic acid 638190-92-8P,  
(2S)-4-[2-[[2-[Ethyl(3-methylphenyl)amino]ethyl]amino]-2-oxoethoxy]- $\alpha$ -methoxybenzenepropanoic acid  
638190-93-9P, (2S)- $\alpha$ -Methoxy-4-[2-oxo-2-[[2-(2-pyridinyl)ethyl]amino]ethoxy]benzenepropanoic acid  
638190-94-0P, (2S)- $\alpha$ -Methoxy-4-[2-oxo-2-[[2-(3-pyridinyl)ethyl]amino]ethoxy]benzenepropanoic acid  
638190-95-1P 638190-96-2P 638190-97-3P  
, (2S)-4-[2-(Cyclobutylamino)-2-oxoethoxy]- $\alpha$ -methoxybenzenepropanoic acid 638190-98-4P  
638190-99-5P 638191-00-1P 638191-01-2P  
, (2S)- $\alpha$ -Methoxy-4-[2-[(3-methylbutyl)amino]-2-oxoethoxy]benzenepropanoic acid 638191-02-3P,  
(2S)-4-[2-(Cyclopentylamino)-2-oxoethoxy]- $\alpha$ -methoxybenzenepropanoic acid 638191-03-4P  
638191-04-5P, (2S)-4-[2-[(2,2,3,3,4,4,4-Heptafluorobutyl)amino]-2-oxoethoxy]- $\alpha$ -methoxybenzenepropanoic acid 638191-08-9P,  
(2S)-4-[2-(Hexylamino)-2-oxoethoxy]- $\alpha$ -methoxybenzenepropanoic acid 638191-09-0P,  
(2S)-4-[2-(Heptylamino)-2-oxoethoxy]- $\alpha$ -methoxybenzenepropanoic acid 638191-10-3P,  
(2S)-4-[2-[(3,3-Dimethylbutyl)amino]-2-oxoethoxy]- $\alpha$ -methoxybenzenepropanoic acid 638191-11-4P  
638191-24-9P, 4-[2-[Cyclohexyl[2-(4-ethylphenyl)ethyl]amino]-2-oxoethoxy]- $\alpha$ -ethoxybenzenepropanoic acid 719277-13-1P,  
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(2S)-3-[4-[2-[(4-Chlorobenzyl)(ethyl)amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoic acid 719277-15-3P, (2S)-2-Ethoxy-3-[4-[2-[ethyl[4-(trifluoromethoxy)benzyl]amino]-2-oxoethoxy]phenyl]propanoic acid 719277-16-4P,  
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(2S)-3-[4-[2-[Butyl[4-(trifluoromethyl)benzyl]amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoic acid **816465-03-9P**,  
 (2S)-3-[4-[2-[(2,4-Difluorobenzyl)(octyl)amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoic acid **816465-07-3P**,  
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 (2S)-3-[4-[2-[Benzyl(methyl)amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoic acid **816465-17-5P**, (2S)-2-Ethoxy-3-[4-[2-[heptyl[(1-methylindol-2-yl)methyl]amino]-2-oxoethoxy]phenyl]propanoic acid **816465-20-0P**,  
 (2S)-3-[4-[2-[(2,3-Dimethoxybenzyl)(heptyl)amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoic acid **816465-23-3P**,  
 (2S)-3-[4-[2-[Butyl(2,3-dimethoxybenzyl)amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoic acid **816465-25-5P**,  
 (2S)-3-[4-[2-[(4-Chlorobenzyl)(4-isopropylbenzyl)amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoic acid **816465-28-8P**,  
 (2S)-3-[4-[2-[(Cyclohexylmethyl)(2,4-difluorobenzyl)amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoic acid **816465-33-5P**,  
 (2S)-2-Ethoxy-3-[4-[2-[ethyl(2-fluorobenzyl)amino]-2-oxoethoxy]phenyl]propanoic acid **816465-35-7P**,  
 (2S)-3-[4-[2-[[4-(Benzyloxy)benzyl](butyl)amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoic acid **816465-37-9P**,  
 (2S)-3-[4-[2-[Bis(4-Chlorobenzyl)amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoic acid **816465-43-7P**, (2S)-3-[4-[2-[(4-tert-Butylbenzyl)(4-chlorobenzyl)amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoic acid **816465-47-1P**, (2S)-3-[4-[2-[(4-Chlorobenzyl)[4-(trifluoromethyl)benzyl]amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoic acid **816465-51-7P**,  
 (2S)-3-[4-[2-[Bis[4-(Trifluoromethyl)benzyl]amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoic acid **816465-55-1P**,  
 (2S)-3-[4-[2-[Benzyl(ethyl)amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoic acid **816465-57-3P**, (2S)-3-[4-[2-[(4-tert-Butylbenzyl)(ethyl)amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoic acid **816465-64-2P**, (2S)-4-[2-(Heptylamino)-2-oxoethoxy]- $\alpha$ -methoxy- $\alpha$ -methylbenzenepropanoic acid **816465-65-3P**, 4-[2-[4-(2-Fluorophenyl)-1-piperazinyl]-2-oxoethoxy]- $\alpha$ -methoxybenzenepropanoic acid **816465-67-5P**,  
 (2S)-3-[2-[2-(4-Ethylphenyl)ethyl]amino]-2-oxoethoxy]- $\alpha$ -methoxybenzenepropanoic acid **817181-62-7P**  
**871731-30-5P**

(preparation of phenoxyacetamide derivs. as modulators of  
**peroxisome** proliferator-activated receptors for  
 treating metabolic disorder)

IT 103-67-3, N-Methylbenzylamine 104-86-9, 4-Chlorobenzylamine  
 109-73-9, n-Butylamine, reactions 111-14-8, Heptanoic acid  
 111-68-2, Heptylamine 112-05-0, Nonanoic acid 122-03-2,  
 4-Isopropylbenzaldehyde 124-07-2, Octanoic acid, reactions  
 619-64-7, 4-Ethylbenzoic acid 939-97-9, 4-tert-Butylbenzaldehyde  
 1521-38-6, 2,3-Dimethoxybenzoic acid 2043-61-0,  
 Cyclohexanecarboxaldehyde 3218-02-8, Aminomethylcyclohexane  
 5437-45-6, Benzyl bromoacetate 14321-27-8, N-Benzyl-N-ethylamine  
 21913-13-3, N,N-Bis(4-chlorobenzyl)amine 24997-83-9,  
 N-Hexyl-2-phenylethylamine 25468-44-4, N-Hexylbenzylamine  
 27421-51-8, 1-Methylindole-2-carboxaldehyde 64567-25-5,  
 N-Ethyl-N-(2-fluorobenzyl)amine 66741-82-0, N-[4-(Benzyloxy)benzyl]-N-butylamine 69957-83-1, N-(4-Chlorobenzyl)-N-ethylamine 72235-52-0, 2,4-Difluorobenzylamine 89763-93-9,  
 2-Fluoro-4-(trifluoromethyl)benzaldehyde 90390-12-8,

N-Ethyl-N-[4-(trifluoromethyl)benzyl]amine 90390-14-0,  
N-Butyl-N-[4-(trifluoromethyl)benzyl]amine 93919-56-3,  
4-(Trifluoromethoxy)benzylamine 145126-91-6,  
N,N-Bis[4-(trifluoromethyl)benzyl]amine 152821-50-6,  
N-(4-tert-Butylbenzyl)-N-ethylamine 202145-03-7,  
N-(4-Chlorobenzyl)-N-[4-(trifluoromethyl)benzyl]amine  
222555-06-8, Ethyl (2S)-2-ethoxy-3-(4-hydroxyphenyl)propanoate  
(reactant; preparation of phenoxyacetamide derivs. as modulators of  
peroxisome proliferator-activated receptors for  
treating metabolic disorder)

L32 ANSWER 2 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:1154649 HCAPLUS

DOCUMENT NUMBER: 142:93514

TITLE: Preparation of phenylpropanoic acid  
derivatives as PPAR $\alpha$  agonists

INVENTOR(S): Li, Lanna; Lindstedt-Alstermark, Eva-Lotte;  
Olsson, Christina

PATENT ASSIGNEE(S): Astrazeneca Ab, Swed.

SOURCE: PCT Int. Appl., 100 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

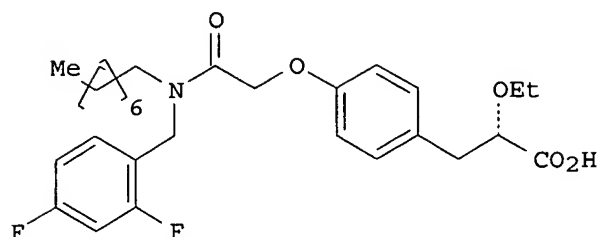
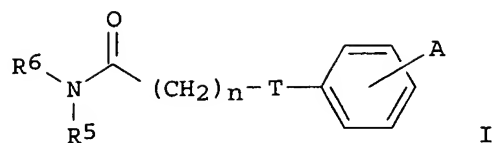
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 5

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004113270	A2	20041229	WO 2004-EP6597	2004 0617
WO 2004113270	A3	20050331		
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AU 2004249409	A1	20041229	AU 2004-249409	2004 0617
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US 2005148656	A1	20050707	US 2003-518777	2004 0617
EP 1675820	A2	20060705	EP 2004-740044	2004 0617
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EP 1676833	A1	20060705	EP 2006-5766	
				2004 0617
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US 2005282822	A1	20051222	US 2004-26806	
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				2005 1212
PRIORITY APPLN. INFO.:			GB 2003-14079	A 2003 0618
			SE 2001-4334	A 2001 1219
			<-- WO 2002-GB5738	W 2002 1218
			<-- WO 2002-GB5744	A 2002 1218
			<-- GB 2002-29931	A 2002 1221
			<-- WO 2003-GB305602	A 2003 1219
			EP 2004-740044	A3 2004 0617
			WO 2004-EP6597	W 2004 0617
			US 2005-499261	A2 2005 0304
OTHER SOURCE(S):	MARPAT 142:93514			
GI				



AB Title compds. represented by the formula I [wherein A = CR<sub>3</sub>(R<sub>4</sub>)CR<sub>1</sub>(R<sub>2</sub>)COR or C(R<sub>3</sub>):C(R<sub>1</sub>)COR; R = H, alkoxy, (alkyl)aryloxy, amino, etc.; R<sub>1</sub> = alkyl, aryl, alkenyl, alkynyl, etc.; R<sub>2</sub> = H, halo, alkyl, (alkyl)aryl; R<sub>3</sub>, R<sub>4</sub> = independently H, alkyl, (alkyl)aryl; T = O, S or a single bond; n = 1-4; R<sub>5</sub>, R<sub>6</sub> = independently selected substituent comprising C, H, N, O, S, Se, P or halo; with provisos; optical isomers and racemates thereof as well as pharmaceutically acceptable salts, prodrugs, solvates and crystalline forms thereof] were prepared as PPAR $\alpha$  agonists. For example, II was given in a multi-step synthesis starting from the reaction of 2,4-difluorobenzylamine with octanoic acid. I had EC<sub>50</sub> values of less than 0.1  $\mu$ mol/L for PPAR $\alpha$  and showed the ration of the EC<sub>50</sub>(PPAR $\gamma$ ) with EC<sub>50</sub>(PPAR $\alpha$ ) is greater than 150:1. Thus, I and their pharmaceutical compns. are useful for the treatment of clin. conditions including lipid disorders (dyslipidemias) whether or not associated with insulin resistance (no data).

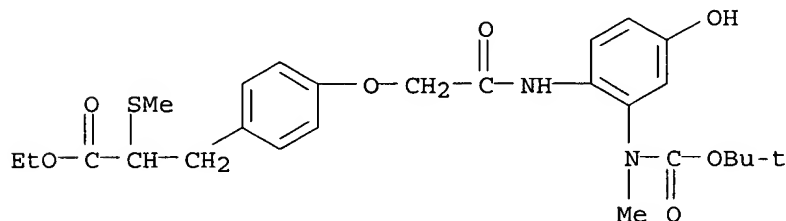
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(preparation of phenylpropanoic acid derivs. as PPAR $\alpha$  agonists)

RN 299176-05-9 HCAPLUS

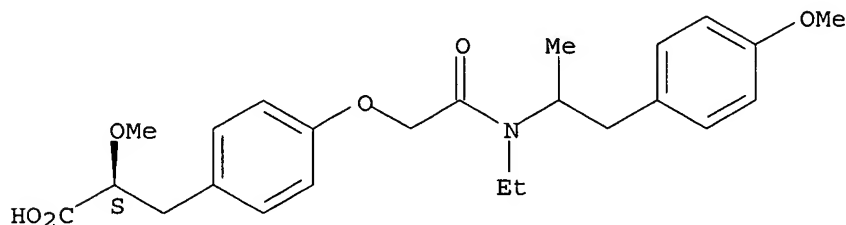
CN Benzenepropanoic acid, 4-[2-[[2-[[[(1,1-dimethylethoxy)carbonyl]methylamino]-4-hydroxyphenyl]amino]-2-oxoethoxy]- $\alpha$ -(methylthio)-, ethyl ester (9CI) (CA INDEX NAME)



RN 638189-90-9 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[ethyl[2-(4-methoxyphenyl)-1-methylethyl]amino]-2-oxoethoxy]- $\alpha$ -methoxy-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

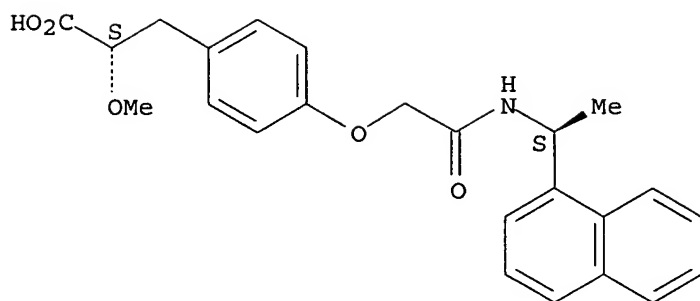


RN 638189-91-0 HCAPLUS

CN Benzenepropanoic acid,  $\alpha$ -methoxy-4-[2-[[[(1S)-1-(1-naphthalenyl)ethyl]amino]-2-oxoethoxy]-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

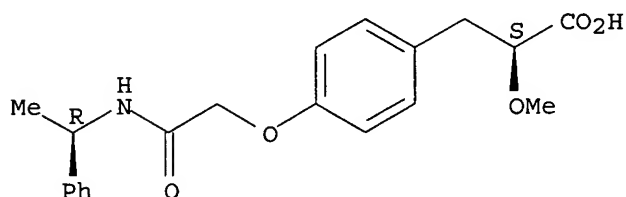




RN 638189-92-1 HCAPLUS

CN Benzenepropanoic acid, α-methoxy-4-[2-oxo-2-[[1R]-1-phenylethyl]amino]ethoxy-, (αS)- (9CI) (CA INDEX NAME)

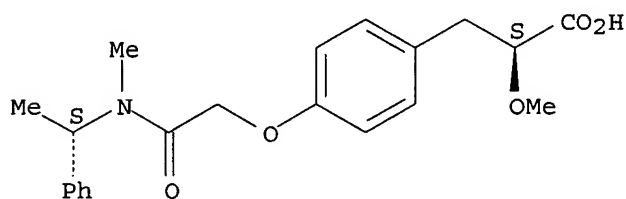
Absolute stereochemistry.



RN 638189-93-2 HCAPLUS

CN Benzenepropanoic acid, α-methoxy-4-[2-[methyl[(1S)-1-phenylethyl]amino]-2-oxoethoxy]-, (αS)- (9CI) (CA INDEX NAME)

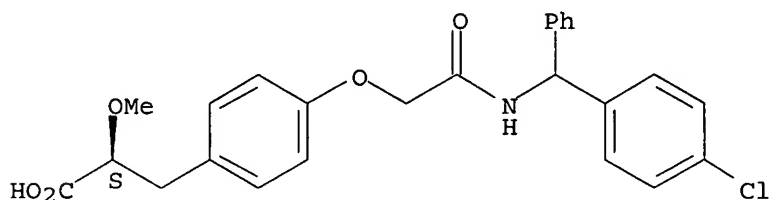
Absolute stereochemistry.



RN 638189-98-7 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[[4-chlorophenyl]phenylmethyl]amino]-2-oxoethoxy]-α-methoxy-, (αS)- (9CI) (CA INDEX NAME)

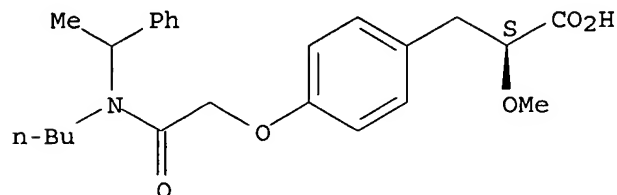
Absolute stereochemistry.



RN 638189-99-8 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[butyl(1-phenylethyl)amino]-2-oxoethoxy]- $\alpha$ -methoxy-, ( $\alpha$ S) - (9CI) (CA INDEX NAME)

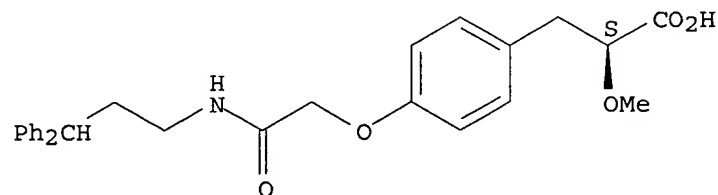
Absolute stereochemistry.



RN 638190-00-8 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[(3,3-diphenylpropyl)amino]-2-oxoethoxy]- $\alpha$ -methoxy-, ( $\alpha$ S) - (9CI) (CA INDEX NAME)

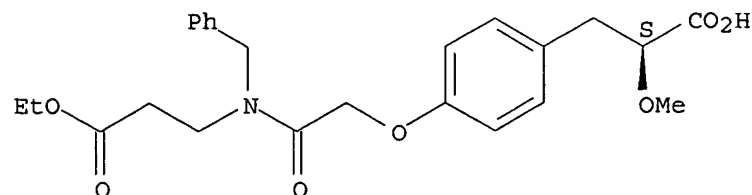
Absolute stereochemistry.



RN 638190-01-9 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[(3-ethoxy-3-oxopropyl)(phenylmethyl)amino]-2-oxoethoxy]- $\alpha$ -methoxy-, ( $\alpha$ S) - (9CI) (CA INDEX NAME)

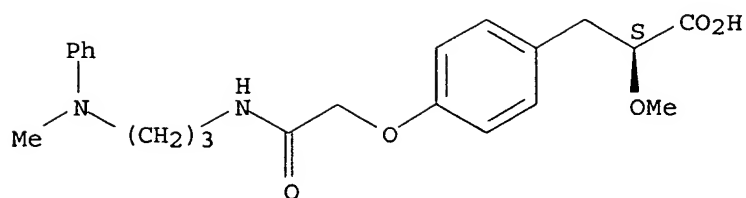
Absolute stereochemistry.



RN 638190-02-0 HCAPLUS

CN Benzenepropanoic acid,  $\alpha$ -methoxy-4-[2-[[3-(methylphenylamino)propyl]amino]-2-oxoethoxy]-, ( $\alpha$ S) - (9CI) (CA INDEX NAME)

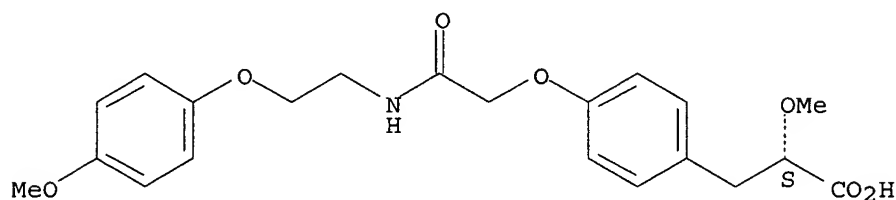
Absolute stereochemistry.



RN 638190-03-1 HCAPLUS

CN Benzenepropanoic acid, α-methoxy-4-[2-[[2-(4-methoxyphenoxy)ethyl]amino]-2-oxoethoxy]-, (αS)- (9CI) (CA INDEX NAME)

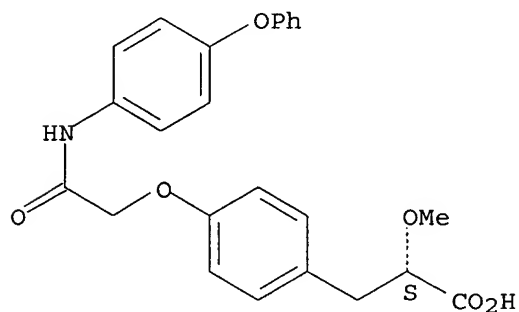
Absolute stereochemistry.



RN 638190-04-2 HCAPLUS

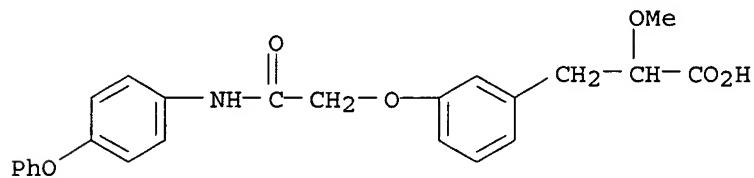
CN Benzenepropanoic acid, α-methoxy-4-[2-oxo-2-[(4-phenoxyphenyl)amino]ethoxy]-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 638190-05-3 HCAPLUS

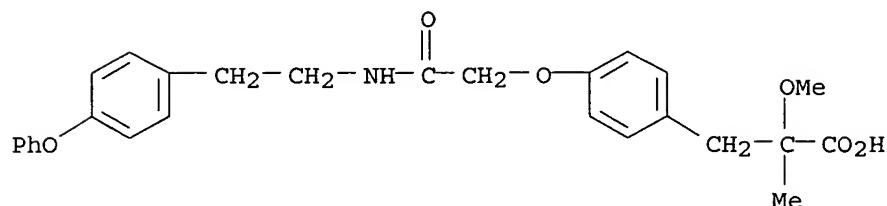
CN Benzenepropanoic acid, α-methoxy-3-[2-oxo-2-[(4-phenoxyphenyl)amino]ethoxy]- (9CI) (CA INDEX NAME)



RN 638190-08-6 HCAPLUS

CN Benzenepropanoic acid, α-methoxy-α-methyl-4-[2-oxo-2-

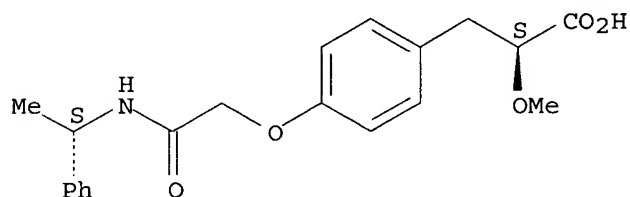
[[2-(4-phenoxyphenyl)ethyl]amino]ethoxy] - (9CI) (CA INDEX NAME)



RN 638190-32-6 HCAPLUS

CN Benzenepropanoic acid,  $\alpha$ -methoxy-4-[2-oxo-2-[[2-(4-phenoxyphenyl)ethyl]amino]ethoxy]-, ( $\alpha$ S) - (9CI) (CA INDEX NAME)

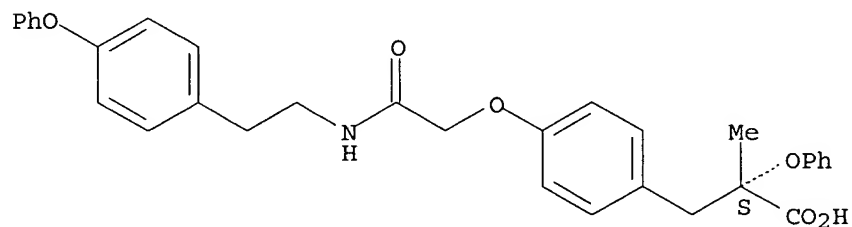
Absolute stereochemistry.



RN 638190-61-1 HCAPLUS

CN Benzenepropanoic acid,  $\alpha$ -methyl-4-[2-oxo-2-[[2-(4-phenoxyphenyl)ethyl]amino]ethoxy]- $\alpha$ -phenoxy-, ( $\alpha$ S) - (9CI) (CA INDEX NAME)

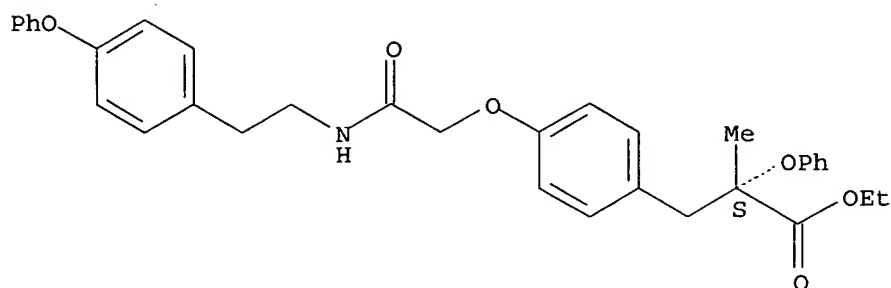
Absolute stereochemistry.



RN 638190-62-2 HCAPLUS

CN Benzenepropanoic acid,  $\alpha$ -methyl-4-[2-oxo-2-[[2-(4-phenoxyphenyl)ethyl]amino]ethoxy]- $\alpha$ -phenoxy-, ethyl ester, ( $\alpha$ S) - (9CI) (CA INDEX NAME)

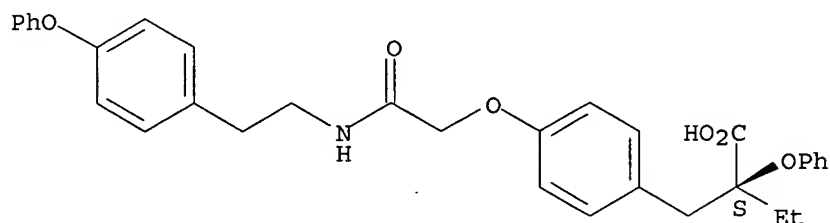
Absolute stereochemistry.



RN 638190-63-3 HCAPLUS

CN Benzenepropanoic acid, α-ethyl-4-[2-oxo-2-[[2-(4-phenoxyphenyl)ethyl]amino]ethoxy]-α-phenoxy-, (αS)-(9CI) (CA INDEX NAME)

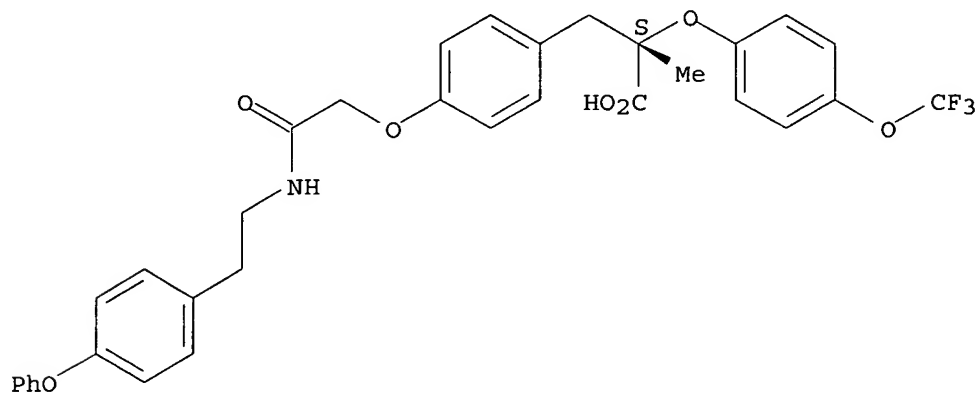
Absolute stereochemistry.



RN 638190-65-5 HCAPLUS

CN Benzenepropanoic acid, α-methyl-4-[2-oxo-2-[[2-(4-phenoxyphenyl)ethyl]amino]ethoxy]-α-[4-(trifluoromethoxy)phenoxy]-, (αS)-(9CI) (CA INDEX NAME)

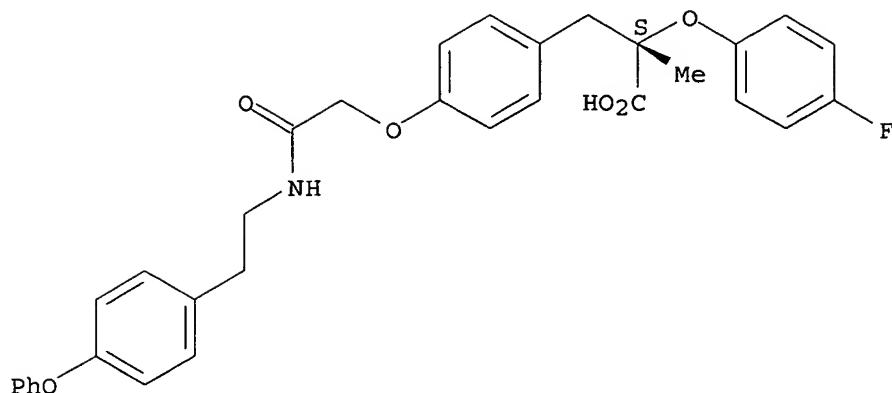
Absolute stereochemistry.



RN 638190-67-7 HCAPLUS

CN Benzenepropanoic acid, α-(4-fluorophenoxy)-α-methyl-4-[2-oxo-2-[[2-(4-phenoxyphenyl)ethyl]amino]ethoxy]-, (αS)-(9CI) (CA INDEX NAME)

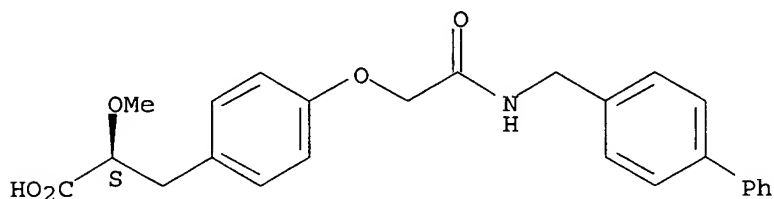
Absolute stereochemistry.



RN 638190-69-9 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[[1,1'-biphenyl]-4-ylmethyl)amino]-2-oxoethoxy]-α-methoxy-, (αS)- (9CI) (CA INDEX NAME)

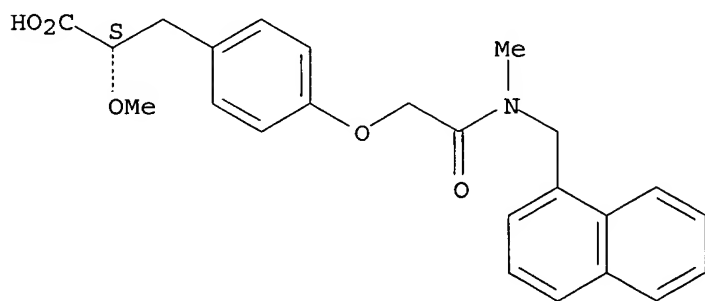
Absolute stereochemistry.



RN 638190-70-2 HCAPLUS

CN Benzenepropanoic acid, α-methoxy-4-[2-[methyl(1-naphthalenylmethyl)amino]-2-oxoethoxy]-, (αS)- (9CI) (CA INDEX NAME)

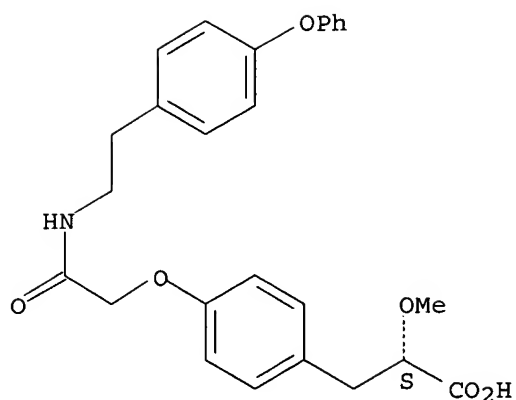
Absolute stereochemistry.



RN 638190-73-5 HCAPLUS

CN Benzenepropanoic acid, α-methoxy-4-[2-oxo-2-[[2-(4-phenoxyphenyl)ethyl]amino]ethoxy]-, (αS)- (9CI) (CA INDEX NAME)

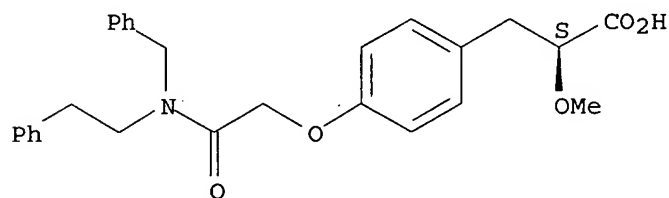
Absolute stereochemistry.



RN 638190-75-7 HCAPLUS

CN Benzenepropanoic acid, α-methoxy-4-[2-oxo-2-[(2-phenylethyl)(phenylmethyl)amino]ethoxy]-, (αS)- (9CI) (CA INDEX NAME)

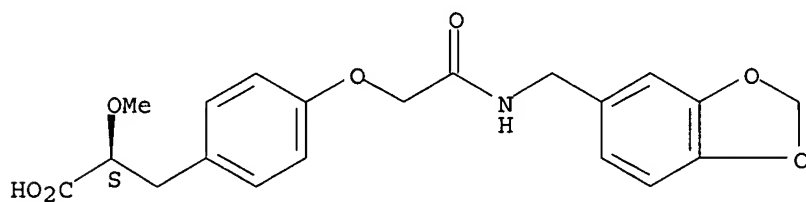
Absolute stereochemistry.



RN 638190-81-5 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[(1,3-benzodioxol-5-ylmethyl)amino]-2-oxoethoxy]-α-methoxy-, (αS)- (9CI) (CA INDEX NAME)

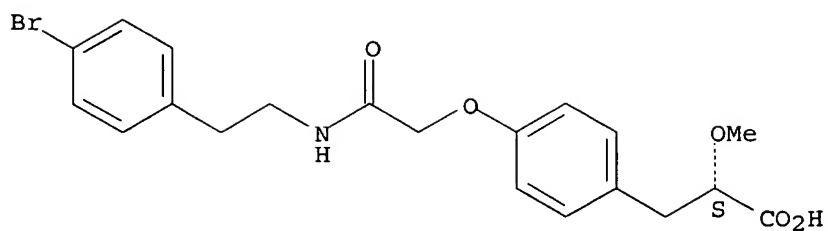
Absolute stereochemistry.



RN 638190-82-6 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[2-(4-bromophenyl)ethyl]amino]-2-oxoethoxy]-α-methoxy-, (αS)- (9CI) (CA INDEX NAME)

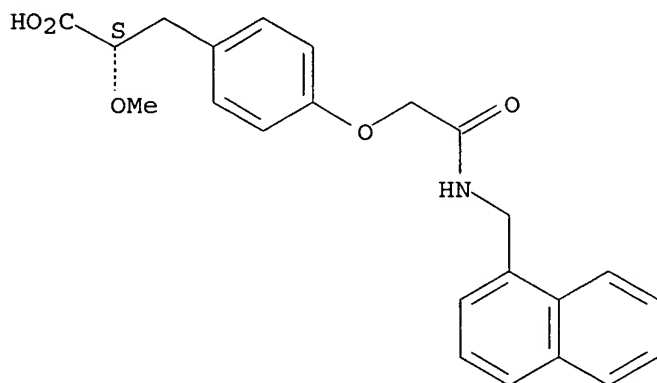
Absolute stereochemistry.



RN 638190-83-7 HCAPLUS

CN Benzenepropanoic acid, α-methoxy-4-[2-[(1-naphthalenylmethyl)amino]-2-oxoethoxy]-, (αS)- (9CI) (CA INDEX NAME)

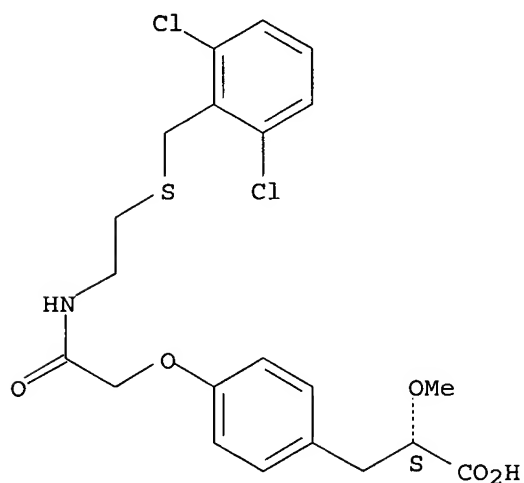
Absolute stereochemistry.



RN 638190-84-8 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[2-[[[2,6-dichlorophenyl)methyl]thio]ethyl]amino]-2-oxoethoxy]-α-methoxy-, (αS)- (9CI) (CA INDEX NAME)

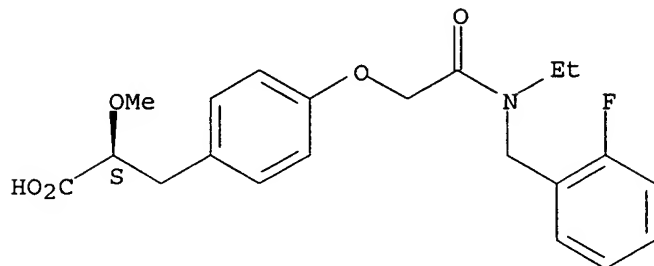
Absolute stereochemistry.





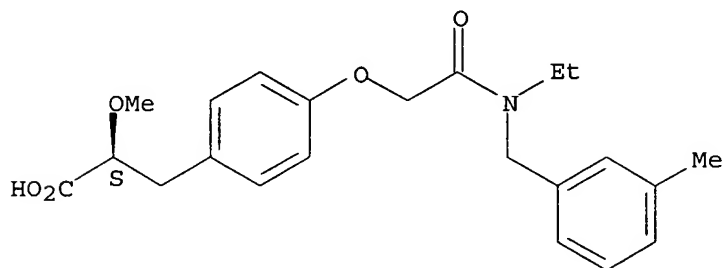
RN 638190-88-2 HCAPLUS  
 CN Benzenepropanoic acid, 4-[2-[ethyl[(2-fluorophenyl)methyl]amino]-2-oxoethoxy]- $\alpha$ -methoxy-, ( $\alpha$ S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.



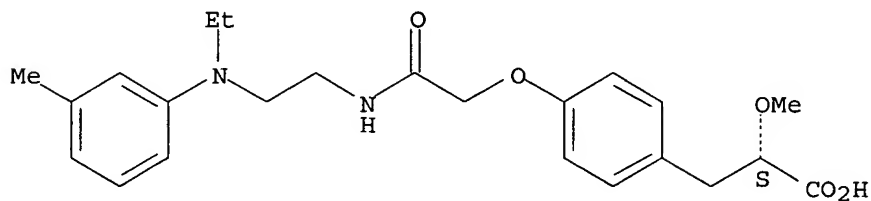
RN 638190-89-3 HCAPLUS  
 CN Benzenepropanoic acid, 4-[2-[ethyl[(3-methylphenyl)methyl]amino]-2-oxoethoxy]- $\alpha$ -methoxy-, ( $\alpha$ S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.



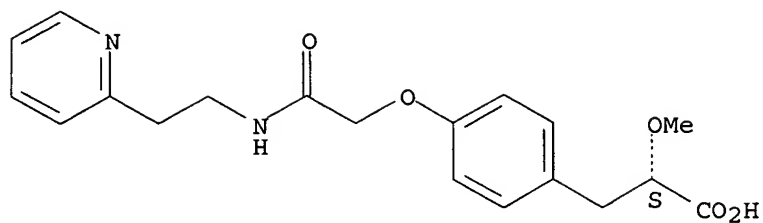
RN 638190-92-8 HCAPLUS  
 CN Benzenepropanoic acid, 4-[2-[[2-[ethyl(3-methylphenyl)amino]ethyl]amino]-2-oxoethoxy]- $\alpha$ -methoxy-, ( $\alpha$ S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 638190-93-9 HCAPLUS  
 CN Benzenepropanoic acid,  $\alpha$ -methoxy-4-[2-oxo-2-[[2-(2-pyridinyl)ethyl]amino]ethoxy]-, ( $\alpha$ S) - (9CI) (CA INDEX NAME)

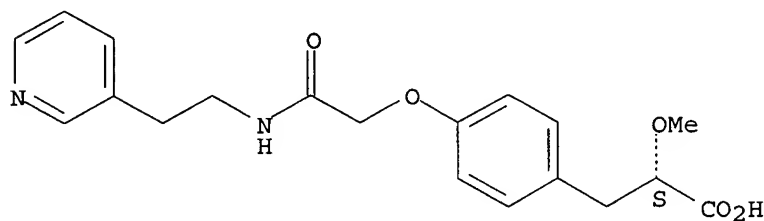
Absolute stereochemistry.



RN 638190-94-0 HCAPLUS

CN Benzenepropanoic acid, α-methoxy-4-[2-oxo-2-[[2-(3-pyridinyl)ethyl]amino]ethoxy]-, (αS)- (9CI) (CA INDEX NAME)

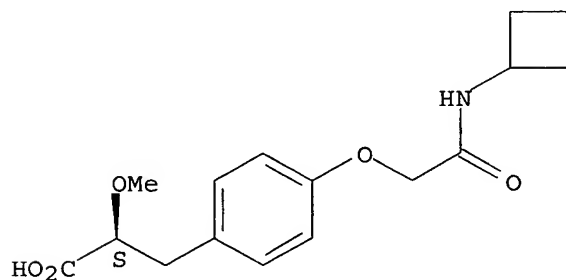
Absolute stereochemistry.



RN 638190-97-3 HCAPLUS

CN Benzenepropanoic acid, 4-[2-(cyclobutylamino)-2-oxoethoxy]-α-methoxy-, (αS)- (9CI) (CA INDEX NAME)

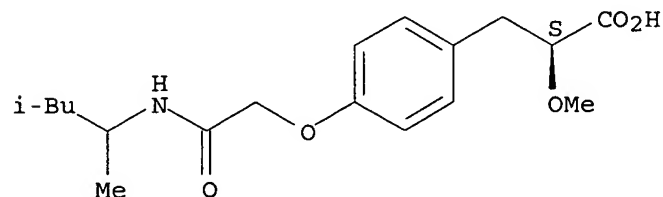
Absolute stereochemistry.



RN 638190-98-4 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[(1,3-dimethylbutyl)amino]-2-oxoethoxy]-α-methoxy-, (αS)- (9CI) (CA INDEX NAME)

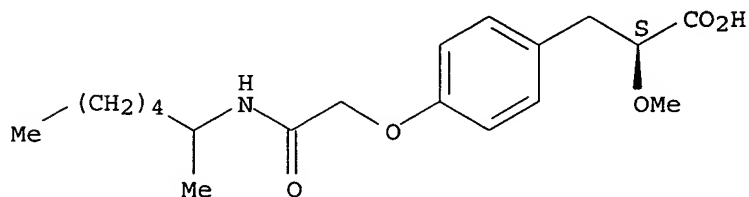
Absolute stereochemistry.



RN 638190-99-5 HCAPLUS

CN Benzenepropanoic acid,  $\alpha$ -methoxy-4-[2-[(1-methylhexyl)amino]-2-oxoethoxy]-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

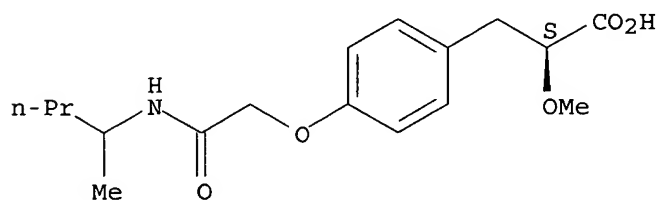
Absolute stereochemistry.



RN 638191-00-1 HCAPLUS

CN Benzenepropanoic acid,  $\alpha$ -methoxy-4-[2-[(1-methylbutyl)amino]-2-oxoethoxy]-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

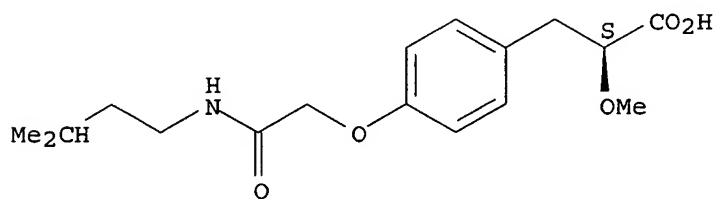
Absolute stereochemistry.



RN 638191-01-2 HCAPLUS

CN Benzenepropanoic acid,  $\alpha$ -methoxy-4-[2-[(3-methylbutyl)amino]-2-oxoethoxy]-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

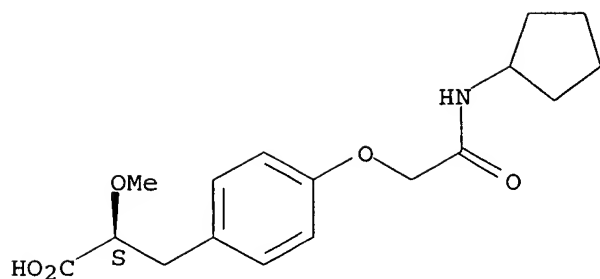
Absolute stereochemistry.



RN 638191-02-3 HCAPLUS

CN Benzenepropanoic acid, 4-[2-(cyclopentylamino)-2-oxoethoxy]- $\alpha$ -methoxy-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

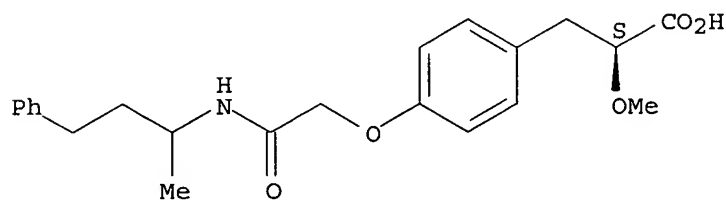
Absolute stereochemistry.



RN 638191-03-4 HCAPLUS

CN Benzenepropanoic acid, α-methoxy-4-[2-[(1-methyl-3-phenylpropyl)amino]-2-oxoethoxy]-, (αS)- (9CI) (CA INDEX NAME)

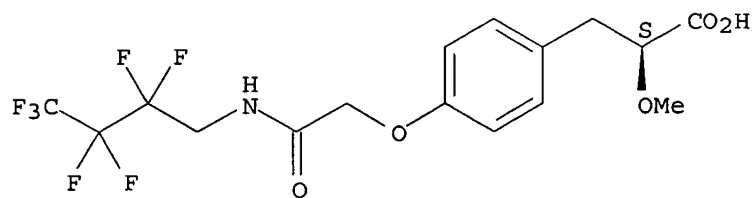
Absolute stereochemistry.



RN 638191-04-5 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[(2,2,3,3,4,4,4-heptafluorobutyl)amino]-2-oxoethoxy]-α-methoxy-, (αS)- (9CI) (CA INDEX NAME)

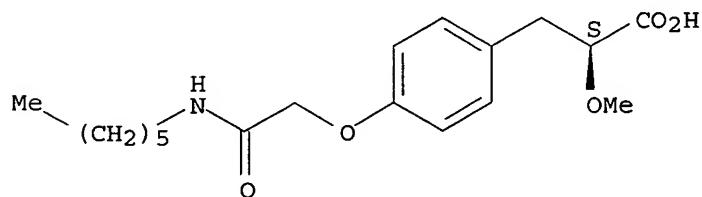
Absolute stereochemistry.



RN 638191-08-9 HCAPLUS

CN Benzenepropanoic acid, 4-[2-(hexylamino)-2-oxoethoxy]-α-methoxy-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



CN Benzenepropanoic acid, 4-[2-(heptylamino)-2-oxoethoxy]- $\alpha$ -methoxy-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

CCCCCCCCNC(=O)COc1ccc(cc1)CSC(=O)O

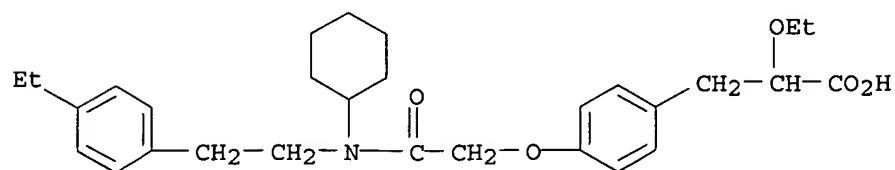
CN Benzenepropanoic acid, 4-[2-[(3,3-dimethylbutyl)amino]-2-oxoethoxy]- $\alpha$ -methoxy-, ( $\alpha$ S) - (9CI) (CA INDEX NAME)

CC(C)CCNC(=O)COc1ccc(cc1)C[C@H](OC)C(=O)O

CN Benzenepropanoic acid, 3-[2-[[cis-4-(1,1-dimethylethyl)cyclohexyl]amino]-2-oxoethoxy]- $\alpha$ -methoxy-(9CI) (CA INDEX NAME)

CC(C)(C)C1CCCCC1NC(=O)COc2ccc(cc2)CC(C)C(=O)O

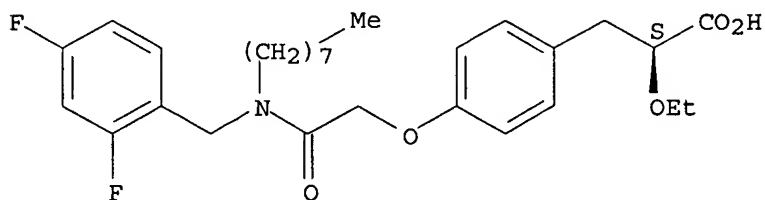
CN	Benzenepropanoic acid, 4-[2-[cyclohexyl[2-(4-ethylphenyl)ethyl]amino]-2-oxoethoxy]- $\alpha$ -ethoxy- (9CI)	(CA
	INDEX NAME)	



RN 816465-03-9 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[[(2,4-difluorophenyl)methyl]octylamin  
o]-2-oxoethoxy]- $\alpha$ -ethoxy-, ( $\alpha$ S)- (9CI) (CA INDEX  
NAME)

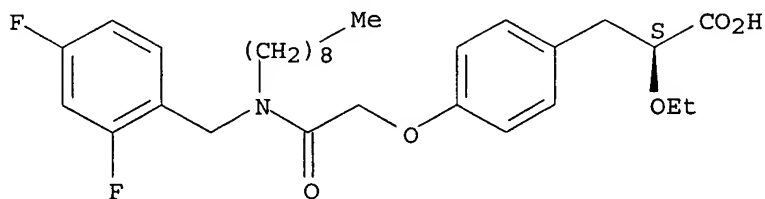
Absolute stereochemistry.



RN 816465-07-3 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[[(2,4-difluorophenyl)methyl]nonylamin  
o]-2-oxoethoxy]- $\alpha$ -ethoxy-, ( $\alpha$ S)- (9CI) (CA INDEX  
NAME)

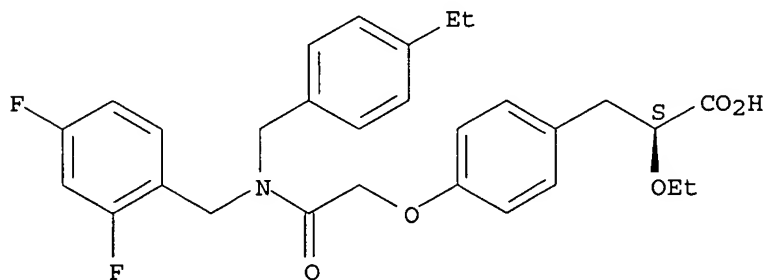
Absolute stereochemistry.



RN 816465-11-9 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[[(2,4-difluorophenyl)methyl][(4-  
ethylphenyl)methyl]amino]-2-oxoethoxy]- $\alpha$ -ethoxy-,  
( $\alpha$ S)- (9CI) (CA INDEX NAME)

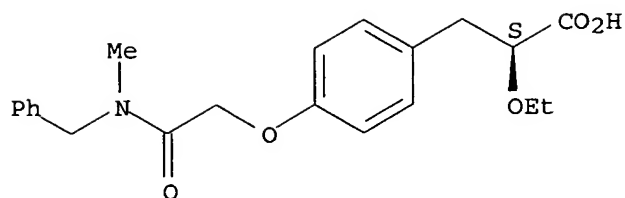
Absolute stereochemistry.



RN 816465-15-3 HCAPLUS

CN Benzenepropanoic acid,  $\alpha$ -ethoxy-4-[2-  
[methyl(phenylmethyl)amino]-2-oxoethoxy]-, ( $\alpha$ S)- (9CI) (CA  
INDEX NAME)

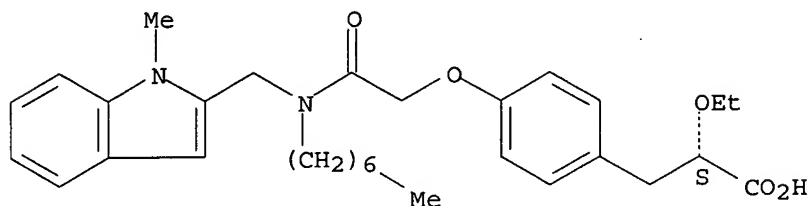
Absolute stereochemistry.



RN 816465-17-5 HCAPLUS

CN Benzenepropanoic acid,  $\alpha$ -ethoxy-4-[2-[heptyl[(1-methyl-1H-indol-2-yl)methyl]amino]-2-oxoethoxy]-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

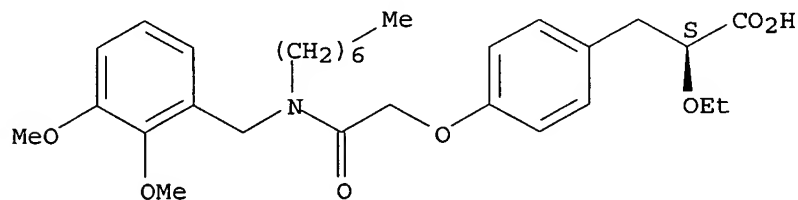
Absolute stereochemistry.



RN 816465-20-0 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[[(2,3-dimethoxyphenyl)methyl]heptylamino]-2-oxoethoxy]- $\alpha$ -ethoxy-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

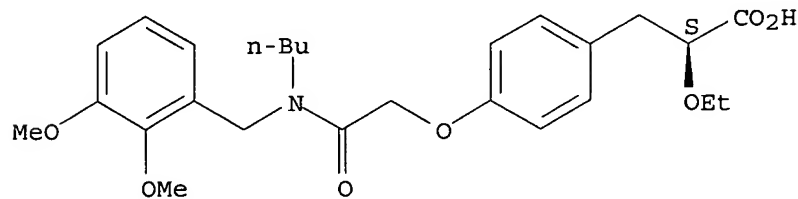
Absolute stereochemistry.



RN 816465-23-3 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[butyl[(2,3-dimethoxyphenyl)methyl]amino]-2-oxoethoxy]- $\alpha$ -ethoxy-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

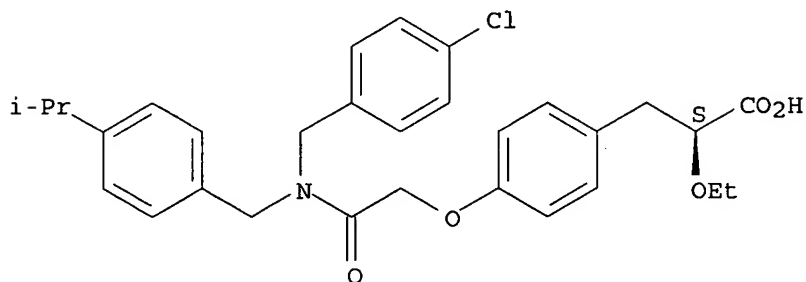


RN 816465-25-5 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[[(4-chlorophenyl)methyl][4-(1-methyl-1H-indol-2-yl)methyl]amino]-2-oxoethoxy]- $\alpha$ -ethoxy-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

methylethyl]phenyl]methyl]amino]-2-oxoethoxy]- $\alpha$ -ethoxy-,  
( $\alpha$ S) - (9CI) (CA INDEX NAME)

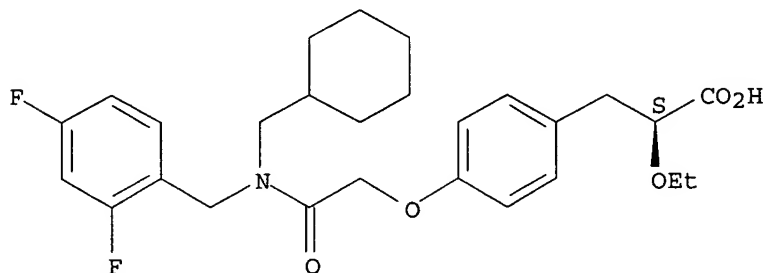
Absolute stereochemistry.



RN 816465-28-8 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[(cyclohexylmethyl)[(2,4-difluorophenyl)methyl]amino]-2-oxoethoxy]- $\alpha$ -ethoxy-,  
( $\alpha$ S) - (9CI) (CA INDEX NAME)

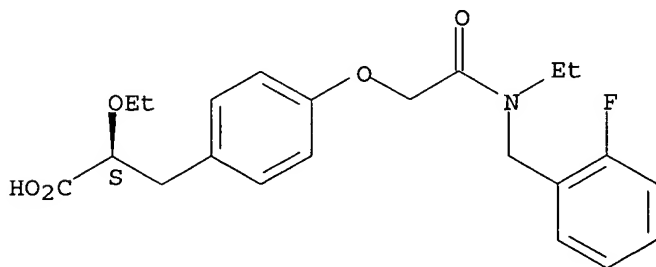
Absolute stereochemistry.



RN 816465-33-5 HCAPLUS

CN Benzenepropanoic acid,  $\alpha$ -ethoxy-4-[2-[ethyl[(2-fluorophenyl)methyl]amino]-2-oxoethoxy]-, ( $\alpha$ S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

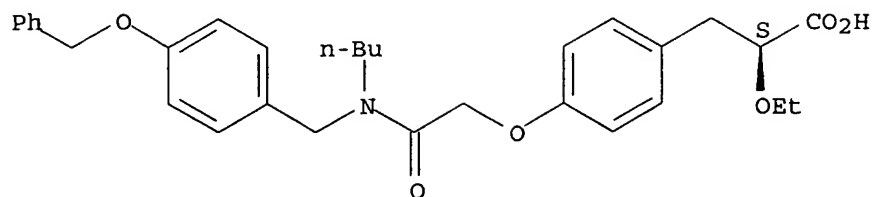


RN 816465-35-7 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[butyl[[4-(phenylmethoxy)phenyl]methyl]amino]-2-oxoethoxy]- $\alpha$ -ethoxy-,  
( $\alpha$ S) - (9CI) (CA INDEX NAME)



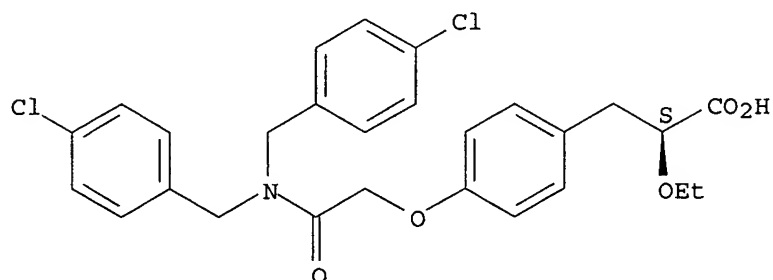
Absolute stereochemistry.



RN 816465-37-9 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[bis[(4-chlorophenyl)methyl]amino]-2-oxoethoxy]-α-ethoxy-, (αS)- (9CI) (CA INDEX NAME)

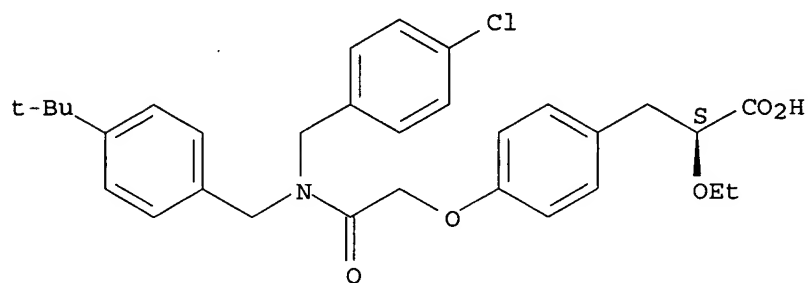
Absolute stereochemistry.



RN 816465-43-7 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[[(4-chlorophenyl)methyl][4-(1,1-dimethylethyl)phenyl]methyl]amino]-2-oxoethoxy]-α-ethoxy-, (αS)- (9CI) (CA INDEX NAME)

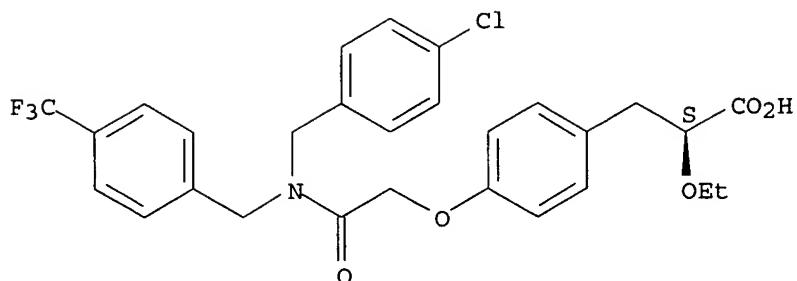
Absolute stereochemistry.



RN 816465-47-1 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[[(4-chlorophenyl)methyl][4-(trifluoromethyl)phenyl]methyl]amino]-2-oxoethoxy]-α-ethoxy-, (αS)- (9CI) (CA INDEX NAME)

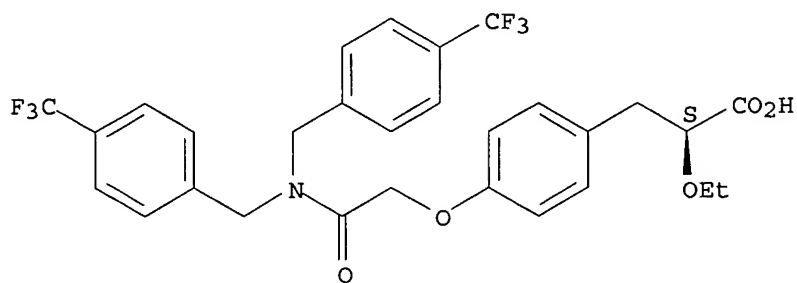
Absolute stereochemistry.



RN 816465-51-7 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[bis[[4-(trifluoromethyl)phenyl]methyl]amino]-2-oxoethoxy]-α-ethoxy-, (αS)- (9CI) (CA INDEX NAME)

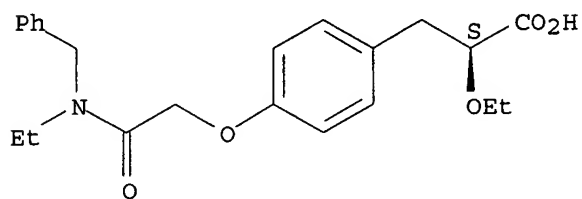
Absolute stereochemistry.



RN 816465-55-1 HCAPLUS

CN Benzenepropanoic acid, α-ethoxy-4-[2-[ethyl(phenylmethyl)amino]-2-oxoethoxy]-, (αS)- (9CI) (CA INDEX NAME)

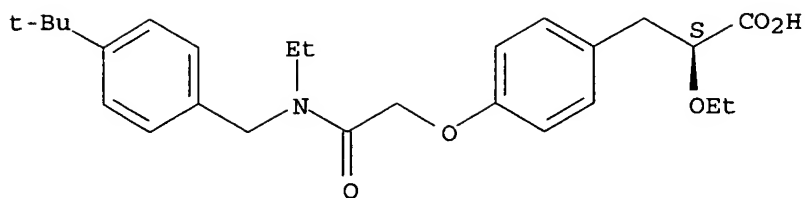
Absolute stereochemistry.



RN 816465-57-3 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[[4-(1,1-dimethylethyl)phenyl]methyl]ethylamino]-2-oxoethoxy]-α-ethoxy-, (αS)- (9CI) (CA INDEX NAME)

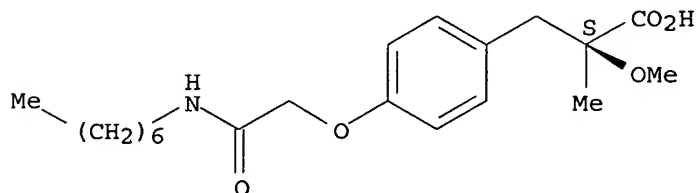
Absolute stereochemistry.



RN 816465-64-2 HCAPLUS

CN Benzenepropanoic acid, 4-[2-(heptylamino)-2-oxoethoxy]-α-methoxy-α-methyl-, (αS)- (9CI) (CA INDEX NAME)

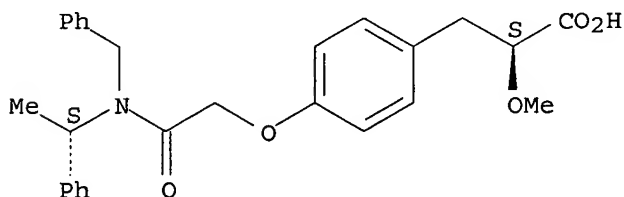
Absolute stereochemistry.



RN 816465-66-4 HCAPLUS

CN Benzenepropanoic acid, α-methoxy-4-[2-oxo-2-[[[(1S)-1-phenylethyl] (phenylmethyl)amino]ethoxy]-, (αS)- (9CI) (CA INDEX NAME)

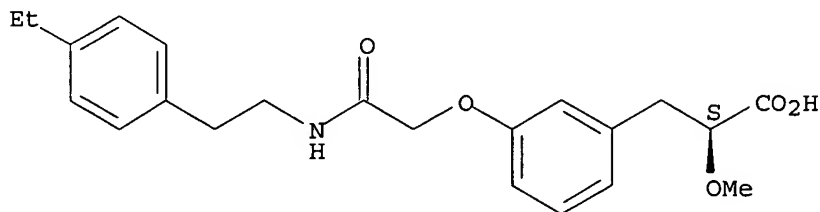
Absolute stereochemistry.



RN 816465-67-5 HCAPLUS

CN Benzenepropanoic acid, 3-[2-[[2-(4-ethylphenyl)ethyl]amino]-2-oxoethoxy]-α-methoxy-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

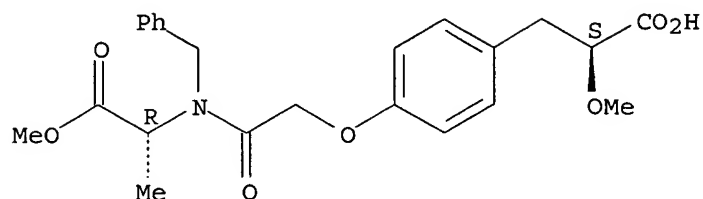


RN 816465-72-2 HCAPLUS

CN Benzenepropanoic acid, α-methoxy-4-[2-[[[(1R)-2-methoxy-1-methyl-2-oxoethyl] (phenylmethyl)amino]-2-oxoethoxy]-, (αS)-

(9CI) (CA INDEX NAME)

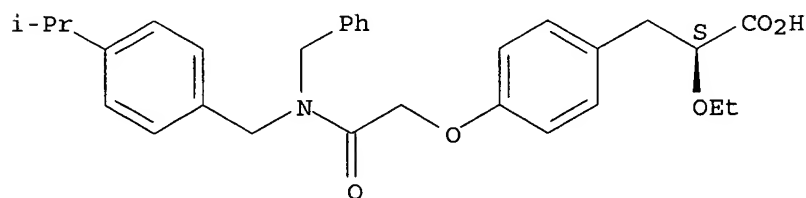
Absolute stereochemistry.



RN 816465-97-1 HCAPLUS

CN Benzenepropanoic acid, α-ethoxy-4-[2-[[[4-(1-methylethyl)phenyl]methyl](phenylmethyl)amino]-2-oxoethoxy]-, (αS)- (9CI) (CA INDEX NAME)

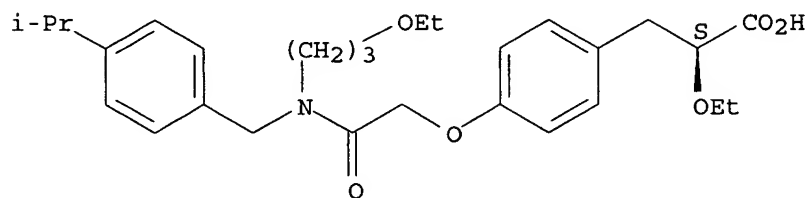
Absolute stereochemistry.



RN 816465-98-2 HCAPLUS

CN Benzenepropanoic acid, α-ethoxy-4-[2-[(3-ethoxypropyl)[[4-(1-methylethyl)phenyl]methyl]amino]-2-oxoethoxy]-, (αS)- (9CI) (CA INDEX NAME)

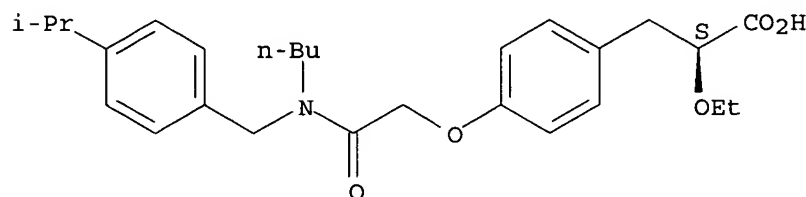
Absolute stereochemistry.



RN 816465-99-3 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[butyl[[4-(1-methylethyl)phenyl]methyl]amino]-2-oxoethoxy]-α-ethoxy-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



Benzenepropanoic acid, 4-[2-[[[(2-chlorophenyl)methyl]heptylamino]-2-oxoethoxy]- $\alpha$ -ethoxy-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

CC(C)C(=O)N(Cc1ccccc1Cl)CCCCC(C)C(=O)COc2ccc(cc2)CSC(C(=O)O)OCC

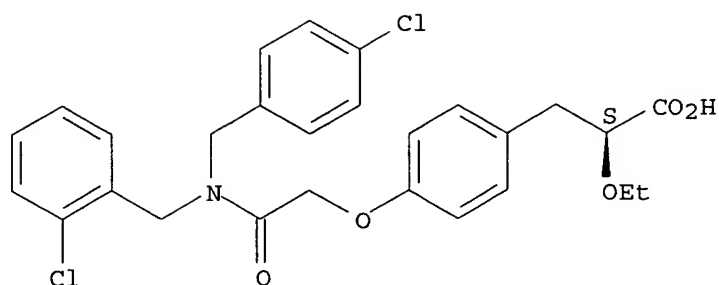
CN Benzenepropanoic acid,  $\alpha$ -ethoxy-4-[2-[heptyl[[4-(1-methylethyl)phenyl]methyl]amino]-2-oxoethoxy]-, ( $\alpha$ S)- (9CI)  
(CA INDEX NAME)

CC(C)C1=CC=C(C=C1)CN(CCCCCC(C)C)C(=O)COc2ccc(cc2)CSC(=O)O[C@H](CC)C(=O)O

CN Benzenepropanoic acid,  $\alpha$ -ethoxy-4-[2-[[2-methoxyphenyl)methyl][4-(1-methylethyl)phenyl)methyl]amino]-2-oxoethoxy]-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

CCOC(=O)[C@H](S)Cc1ccc(OCC(=O)NCCc2cc(OC)ccc2)cc1

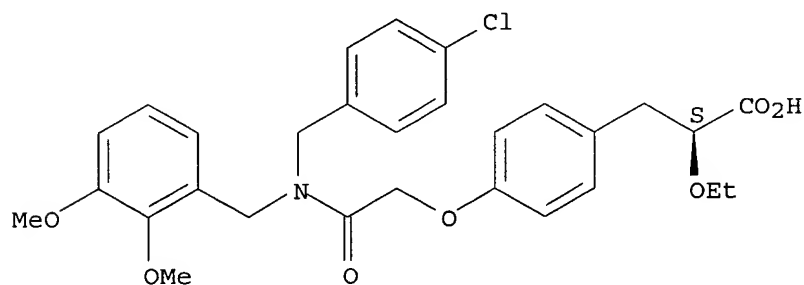
CN Benzenepropanoic acid, 4-[2-[[[(2-chlorophenyl)methyl][(4-chlorophenyl)methyl]amino]-2-oxoethoxy]- $\alpha$ -ethoxy-, (aS)- (9CI) (CA INDEX NAME)



RN 816466-05-4 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[[4-chlorophenyl)methyl][(2,3-dimethoxyphenyl)methyl]amino]-2-oxoethoxy]-α-ethoxy-, (αS) - (9CI) (CA INDEX NAME)

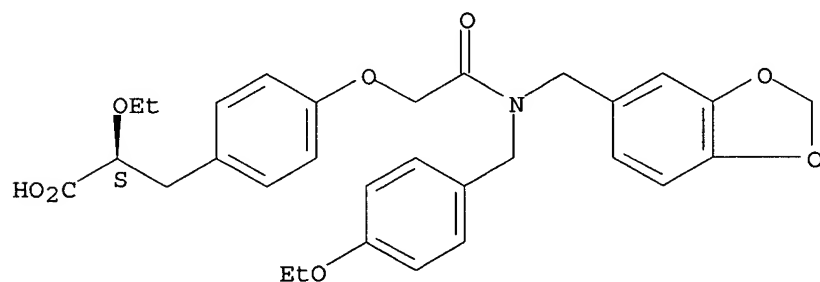
Absolute stereochemistry.



RN 816466-06-5 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[(1,3-benzodioxol-5-yl)methyl][(4-ethoxyphenyl)methyl]amino]-2-oxoethoxy]-α-ethoxy-, (αS) - (9CI) (CA INDEX NAME)

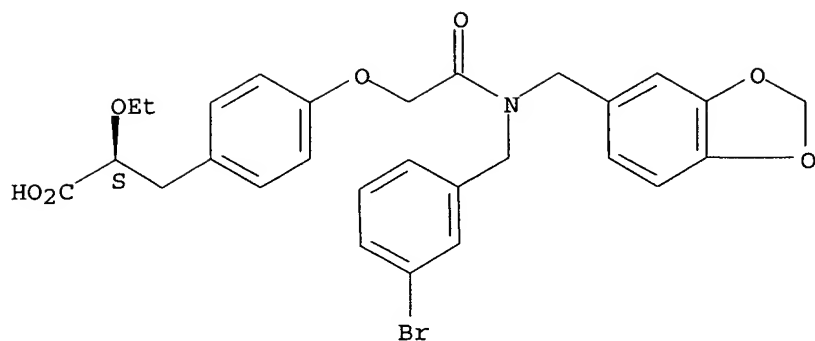
Absolute stereochemistry.



RN 816466-07-6 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[(1,3-benzodioxol-5-yl)methyl][(3-bromophenyl)methyl]amino]-2-oxoethoxy]-α-ethoxy-, (αS) - (9CI) (CA INDEX NAME)

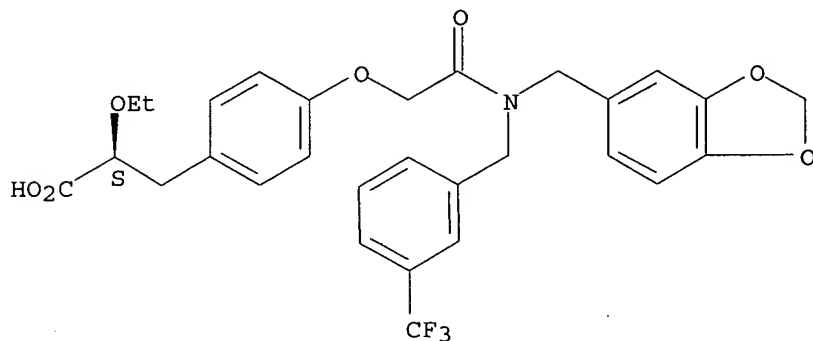
Absolute stereochemistry.



RN 816466-08-7 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[(1,3-benzodioxol-5-ylmethyl)[[3-(trifluoromethyl)phenyl]methyl]amino]-2-oxoethoxy]-α-ethoxy-, (αS)- (9CI) (CA INDEX NAME)

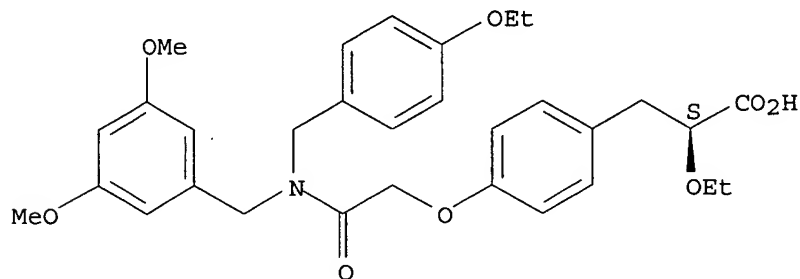
Absolute stereochemistry.



RN 816466-09-8 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[[3,5-dimethoxyphenyl)methyl][(4-ethoxyphenyl)methyl]amino]-2-oxoethoxy]-α-ethoxy-, (αS)- (9CI) (CA INDEX NAME)

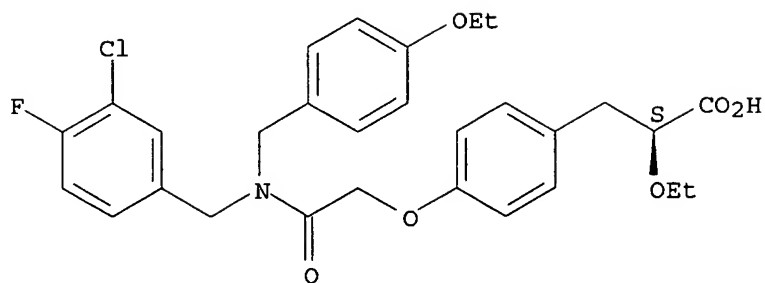
Absolute stereochemistry.



RN 816466-10-1 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[[3-chloro-4-fluorophenyl)methyl][(4-ethoxyphenyl)methyl]amino]-2-oxoethoxy]-α-ethoxy-, (αS)- (9CI) (CA INDEX NAME)

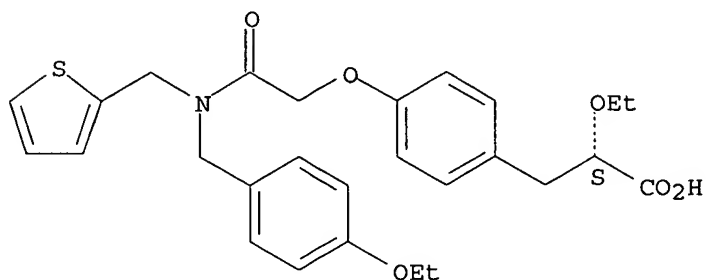
Absolute stereochemistry.



RN 816466-11-2 HCAPLUS

CN Benzenepropanoic acid, α-ethoxy-4-[2-[[4-ethoxyphenyl)methyl] (2-thienylmethyl)amino]-2-oxoethoxy]-, (αS) - (9CI) (CA INDEX NAME)

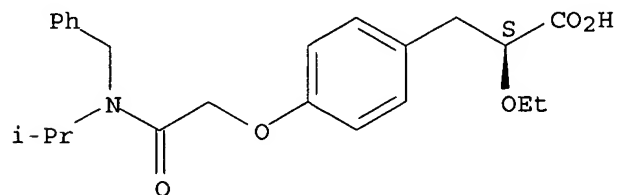
Absolute stereochemistry.



RN 816466-12-3 HCAPLUS

CN Benzenepropanoic acid, α-ethoxy-4-[2-[(1-methylethyl)(phenylmethyl)amino]-2-oxoethoxy]-, (αS) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

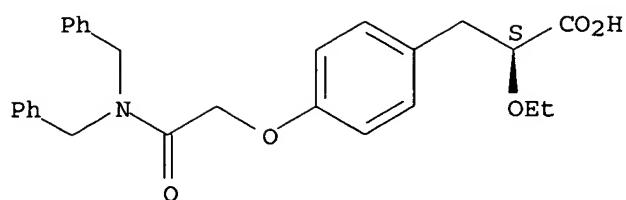


RN 816466-13-4 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[bis(phenylmethyl)amino]-2-oxoethoxy]-α-ethoxy-, (αS) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

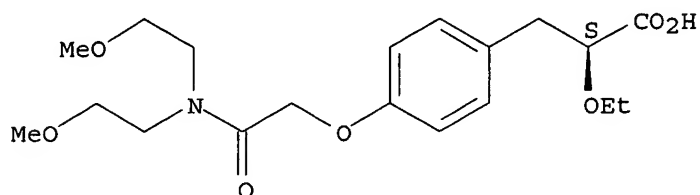




RN 816466-14-5 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[bis(2-methoxyethyl)amino]-2-oxoethoxy]-α-ethoxy-, (αS)-(9CI) (CA INDEX NAME)

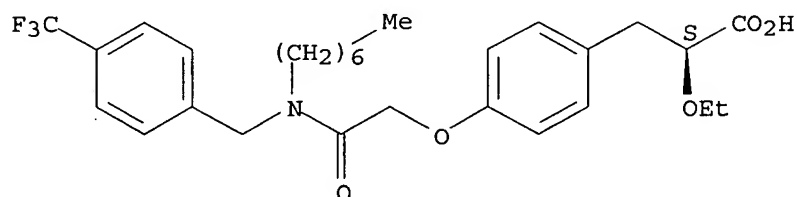
Absolute stereochemistry.



RN 816466-15-6 HCAPLUS

CN Benzenepropanoic acid, α-ethoxy-4-[2-[heptyl[[4-(trifluoromethyl)phenyl]methyl]amino]-2-oxoethoxy]-, (αS)-(9CI) (CA INDEX NAME)

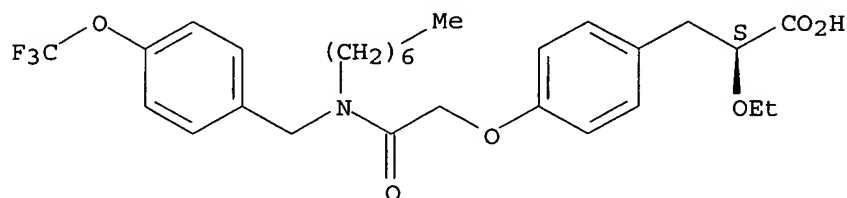
Absolute stereochemistry.



RN 816466-16-7 HCAPLUS

CN Benzenepropanoic acid, α-ethoxy-4-[2-[heptyl[[4-(trifluoromethoxy)phenyl]methyl]amino]-2-oxoethoxy]-, (αS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

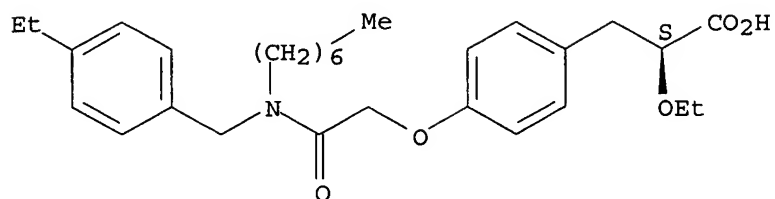


RN 816466-17-8 HCAPLUS

CN Benzenepropanoic acid, α-ethoxy-4-[2-[[[4-ethylphenyl]methyl]heptylamino]-2-oxoethoxy]-, (αS)-(9CI)

(CA INDEX NAME)

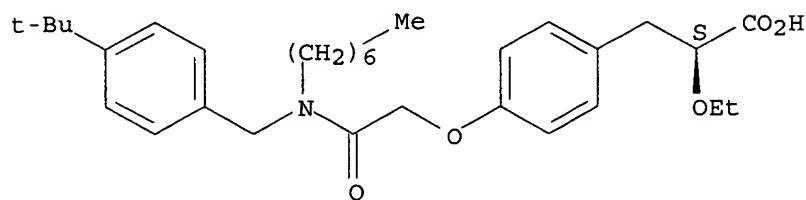
Absolute stereochemistry.



RN 816466-18-9 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[[4-(1,1-dimethylethyl)phenyl]methyl]heptylamino]-2-oxoethoxy]-α-ethoxy-, (αS)- (9CI) (CA INDEX NAME)

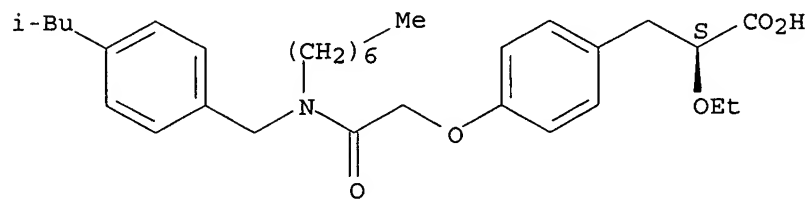
Absolute stereochemistry.



RN 816466-19-0 HCAPLUS

CN Benzenepropanoic acid, α-ethoxy-4-[2-[heptyl[[4-(2-methylpropyl)phenyl]methyl]amino]-2-oxoethoxy]-, (αS)- (9CI) (CA INDEX NAME)

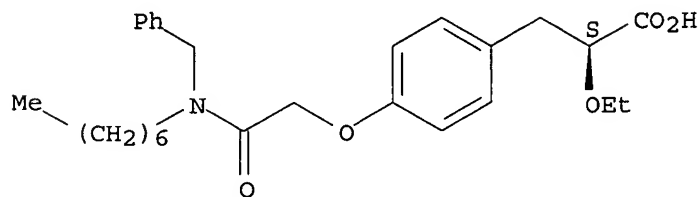
Absolute stereochemistry.



RN 816466-20-3 HCAPLUS

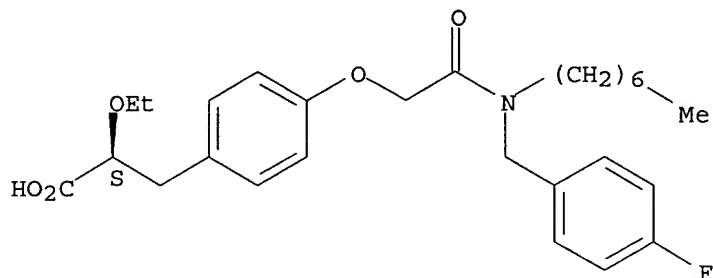
CN Benzenepropanoic acid, α-ethoxy-4-[2-[heptyl(phenylmethyl)amino]-2-oxoethoxy]-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



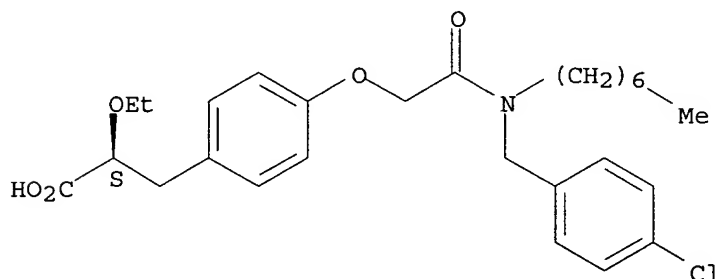
RN 816466-21-4 HCAPLUS  
 CN Benzenepropanoic acid,  $\alpha$ -ethoxy-4-[2-[[[4-fluorophenyl)methyl]heptylamino]-2-oxoethoxy]-, ( $\alpha$ S)- (9CI)  
 (CA INDEX NAME)

Absolute stereochemistry.



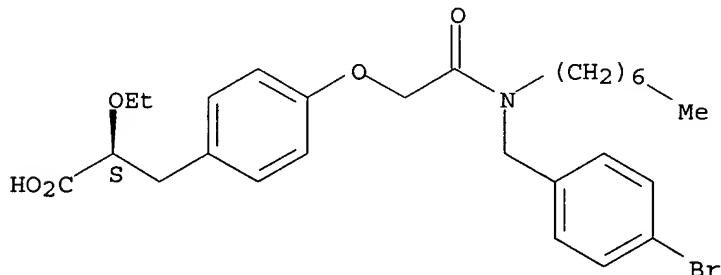
RN 816466-22-5 HCAPLUS  
 CN Benzenepropanoic acid, 4-[2-[[[4-chlorophenyl)methyl]heptylamino]-2-oxoethoxy]- $\alpha$ -ethoxy-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



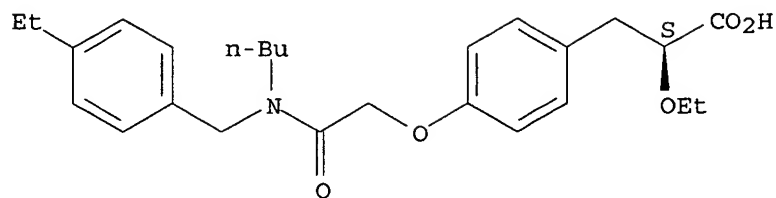
RN 816466-23-6 HCAPLUS  
 CN Benzenepropanoic acid, 4-[2-[[[4-bromophenyl)methyl]heptylamino]-2-oxoethoxy]- $\alpha$ -ethoxy-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 816466-24-7 HCAPLUS  
 CN Benzenepropanoic acid, 4-[2-[butyl[(4-ethylphenyl)methyl]amino]-2-oxoethoxy]- $\alpha$ -ethoxy-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

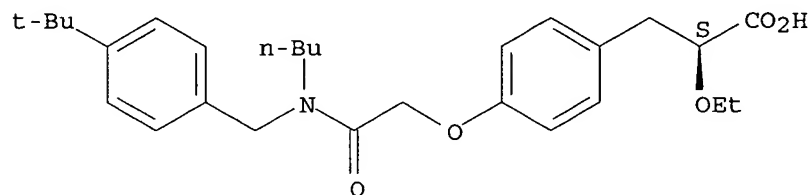
Absolute stereochemistry.



RN 816466-25-8 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[butyl[[4-(1,1-dimethylethyl)phenyl]methyl]amino]-2-oxoethoxy]-α-ethoxy-, (αS) - (9CI) (CA INDEX NAME)

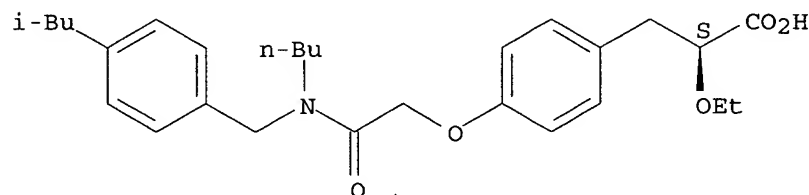
Absolute stereochemistry.



RN 816466-26-9 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[butyl[[4-(2-methylpropyl)phenyl]methyl]amino]-2-oxoethoxy]-α-ethoxy-, (αS) - (9CI) (CA INDEX NAME)

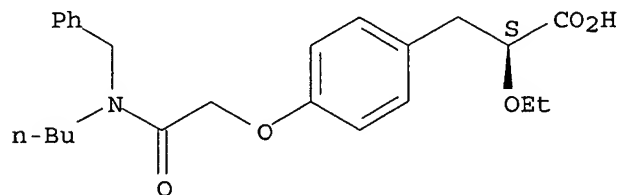
Absolute stereochemistry.



RN 816466-27-0 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[butyl(phenylmethyl)amino]-2-oxoethoxy]-α-ethoxy-, (αS) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

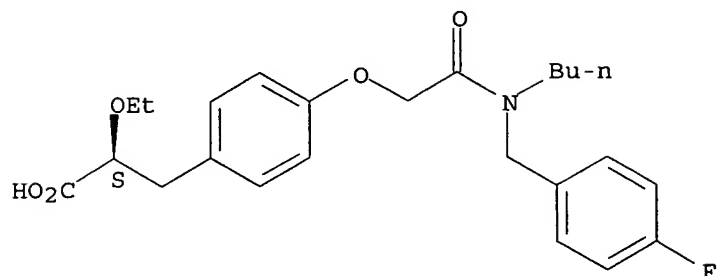


RN 816466-28-1 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[butyl[(4-fluorophenyl)methyl]amino]-2-oxoethoxy]-α-ethoxy-, (αS) - (9CI) (CA INDEX NAME)

oxoethoxy]- $\alpha$ -ethoxy-, ( $\alpha$ S) - (9CI) (CA INDEX NAME)

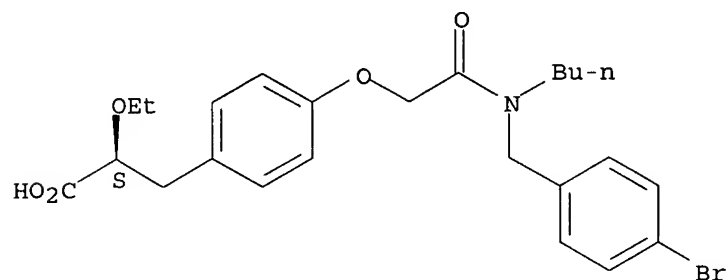
Absolute stereochemistry.



RN 816466-29-2 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[[4-bromophenyl)methyl]butylamino]-2-oxoethoxy]- $\alpha$ -ethoxy-, ( $\alpha$ S) - (9CI) (CA INDEX NAME)

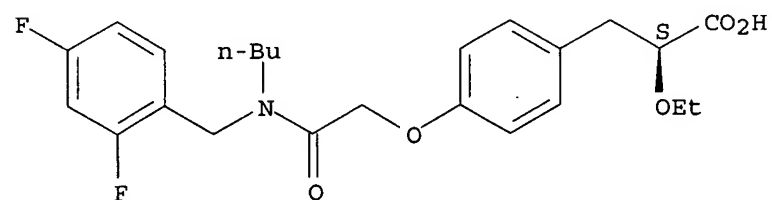
Absolute stereochemistry.



RN 816466-30-5 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[butyl[(2,4-difluorophenyl)methyl]amino]-2-oxoethoxy]- $\alpha$ -ethoxy-, ( $\alpha$ S) - (9CI) (CA INDEX NAME)

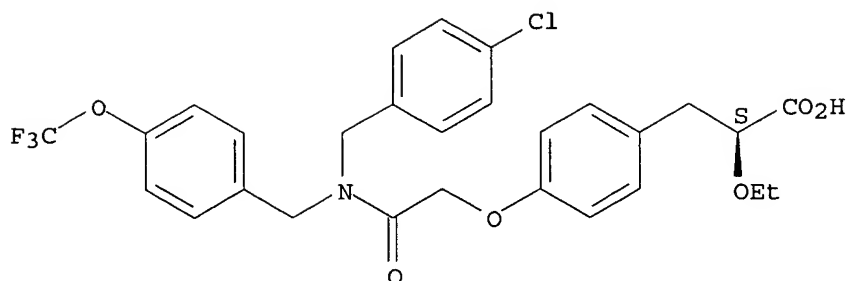
Absolute stereochemistry.



RN 816466-31-6 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[[4-chlorophenyl)methyl][4-(trifluoromethoxy)phenyl)methyl]amino]-2-oxoethoxy]- $\alpha$ -ethoxy-, ( $\alpha$ S) - (9CI) (CA INDEX NAME)

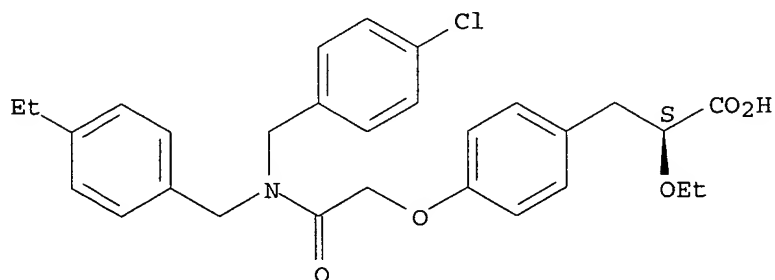
Absolute stereochemistry.



RN 816466-32-7 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[[4-chlorophenyl)methyl][4-ethylphenyl)methyl]amino]-2-oxoethoxy]- $\alpha$ -ethoxy-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

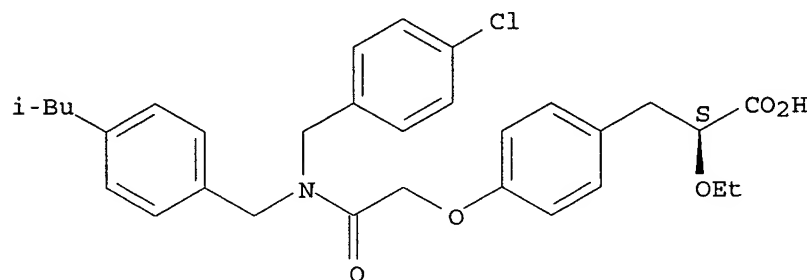
Absolute stereochemistry.



RN 816466-33-8 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[[4-chlorophenyl)methyl][4-(2-methylpropyl)phenyl)methyl]amino]-2-oxoethoxy]- $\alpha$ -ethoxy-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

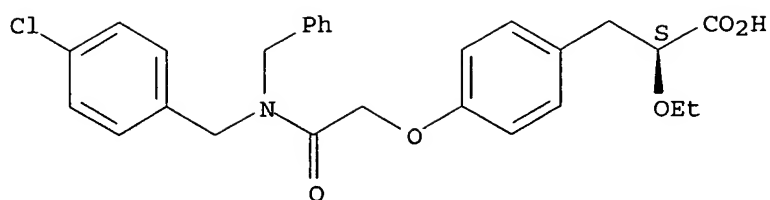
Absolute stereochemistry.



RN 816466-34-9 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[[4-chlorophenyl)methyl](phenylmethyl)amino]-2-oxoethoxy]- $\alpha$ -ethoxy-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

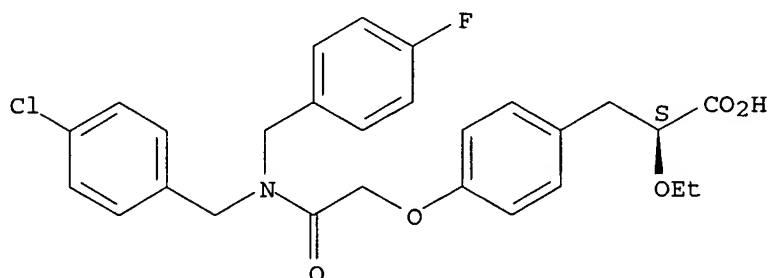
Absolute stereochemistry.



RN 816466-35-0 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[[4-chlorophenyl)methyl][(4-fluorophenyl)methyl]amino]-2-oxoethoxy]-α-ethoxy-, (αS)- (9CI) (CA INDEX NAME)

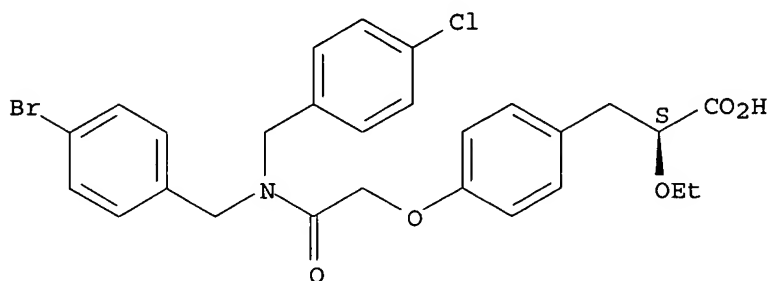
Absolute stereochemistry.



RN 816466-36-1 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[[4-bromophenyl)methyl][(4-chlorophenyl)methyl]amino]-2-oxoethoxy]-α-ethoxy-, (αS)- (9CI) (CA INDEX NAME)

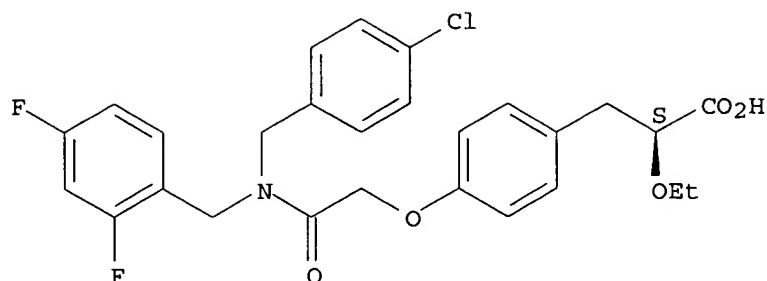
Absolute stereochemistry.



RN 816466-37-2 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[[4-chlorophenyl)methyl][(2,4-difluorophenyl)methyl]amino]-2-oxoethoxy]-α-ethoxy-, (αS)- (9CI) (CA INDEX NAME)

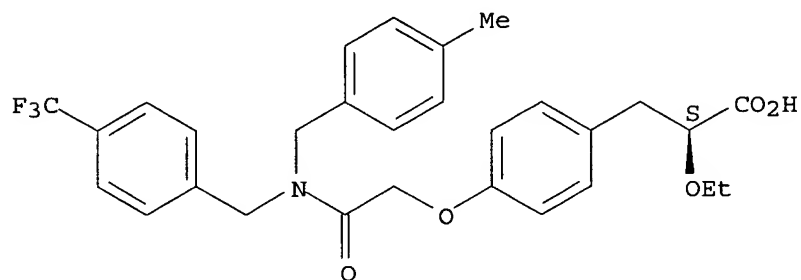
Absolute stereochemistry.



RN 816466-38-3 HCAPLUS

CN Benzenepropanoic acid,  $\alpha$ -ethoxy-4-[2-[[[4-methylphenyl)methyl][4-(trifluoromethyl)phenyl)methyl]amino]-2-oxoethoxy]-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

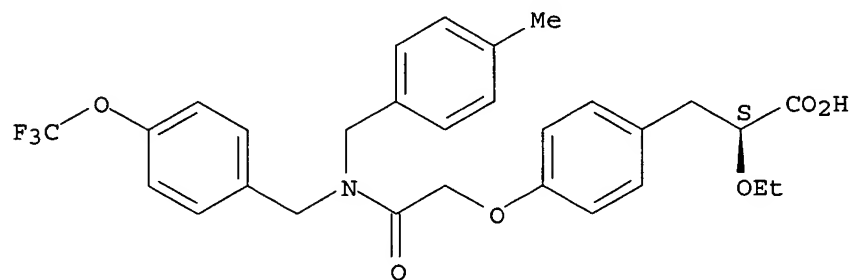
Absolute stereochemistry.



RN 816466-39-4 HCAPLUS

CN Benzenepropanoic acid,  $\alpha$ -ethoxy-4-[2-[[[4-methylphenyl)methyl][4-(trifluoromethoxy)phenyl)methyl]amino]-2-oxoethoxy]-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

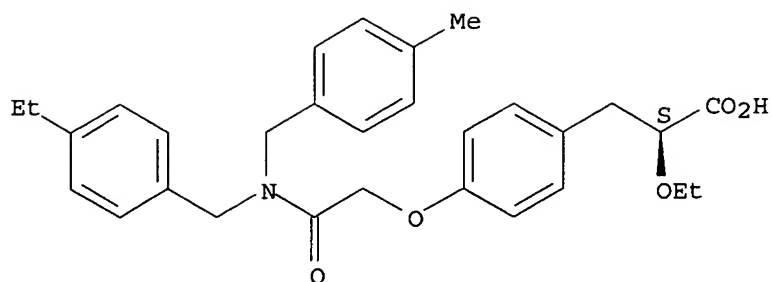


RN 816466-40-7 HCAPLUS

CN Benzenepropanoic acid,  $\alpha$ -ethoxy-4-[2-[[[4-ethylphenyl)methyl][4-(4-methylphenyl)methyl]amino]-2-oxoethoxy]-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

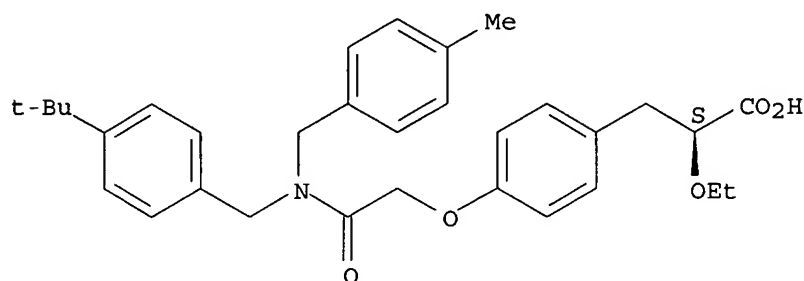




RN 816466-41-8 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[[4-(1,1-dimethylethyl)phenyl]methyl][(4-methylphenyl)methyl]amino]-2-oxoethoxy]- $\alpha$ -ethoxy-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

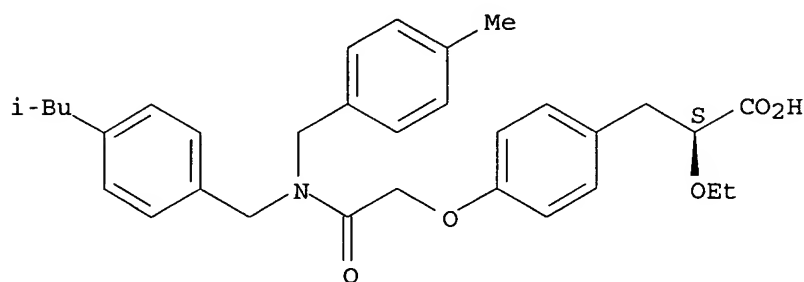
Absolute stereochemistry.



RN 816466-42-9 HCAPLUS

CN Benzenepropanoic acid,  $\alpha$ -ethoxy-4-[2-[[[4-(2-methylpropyl)phenyl]methyl]amino]-2-oxoethoxy]-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

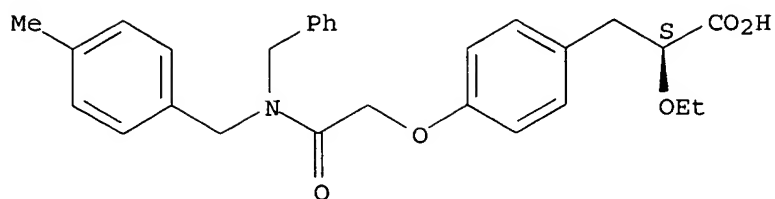
Absolute stereochemistry.



RN 816466-43-0 HCAPLUS

CN Benzenepropanoic acid,  $\alpha$ -ethoxy-4-[2-[[[4-(2-methylpropyl)phenyl]methyl]amino]-2-oxoethoxy]-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

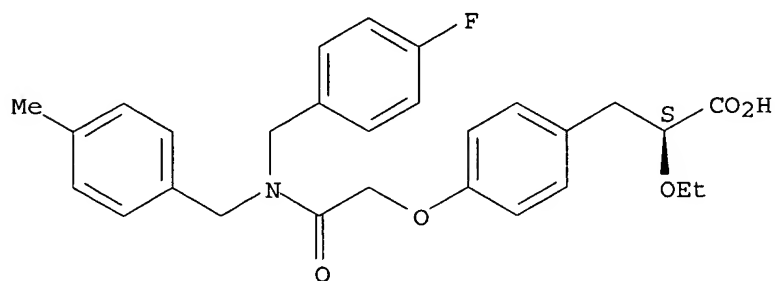
Absolute stereochemistry.



RN 816466-44-1 HCAPLUS

CN Benzenepropanoic acid,  $\alpha$ -ethoxy-4-[2-[[[4-(4-fluorophenyl)methyl]amino]-2-oxoethoxy]-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

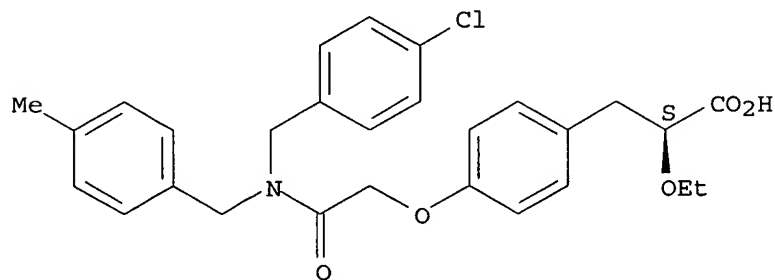
Absolute stereochemistry.



RN 816466-45-2 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[[4-(4-chlorophenyl)methyl]amino]-2-oxoethoxy]- $\alpha$ -ethoxy-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

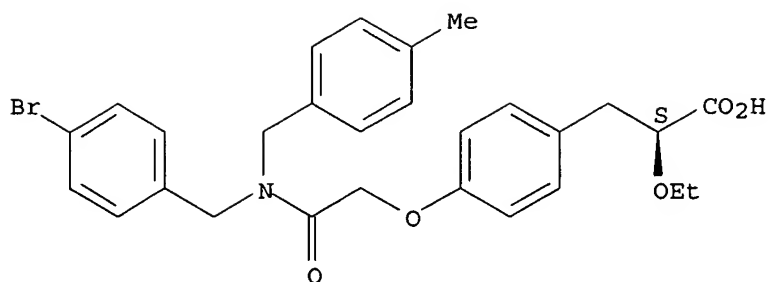
Absolute stereochemistry.



RN 816466-46-3 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[[4-(4-bromophenyl)methyl]amino]-2-oxoethoxy]- $\alpha$ -ethoxy-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

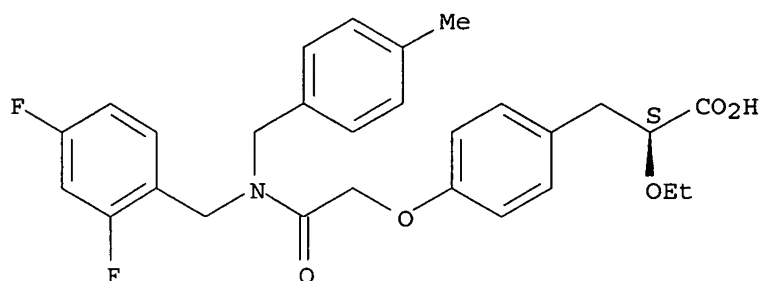
Absolute stereochemistry.



RN 816466-47-4 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[[(2,4-difluorophenyl)methyl][(4-methylphenyl)methyl]amino]-2-oxoethoxy]-α-ethoxy-, (αS)- (9CI) (CA INDEX NAME)

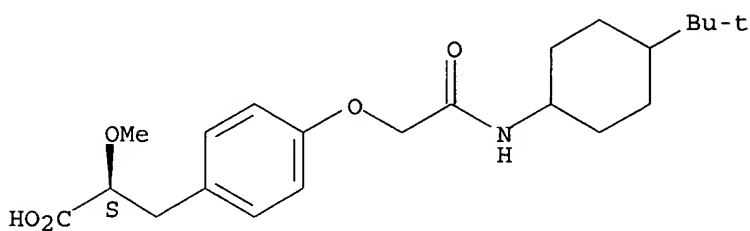
Absolute stereochemistry.



RN 817181-61-6 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[4-(1,1-dimethylethyl)cyclohexyl]amino]-2-oxoethoxy]-α-methoxy-, (αS)- (9CI) (CA INDEX NAME)

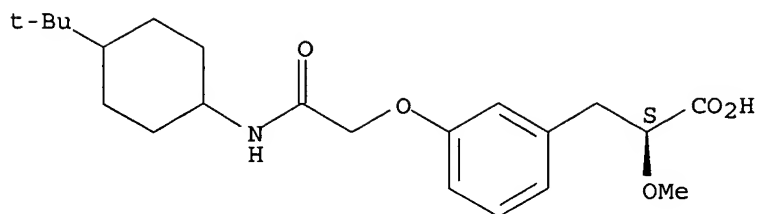
Absolute stereochemistry.



RN 817181-62-7 HCAPLUS

CN Benzenepropanoic acid, 3-[2-[[4-(1,1-dimethylethyl)cyclohexyl]amino]-2-oxoethoxy]-α-methoxy-, (αS)- (9CI) (CA INDEX NAME)

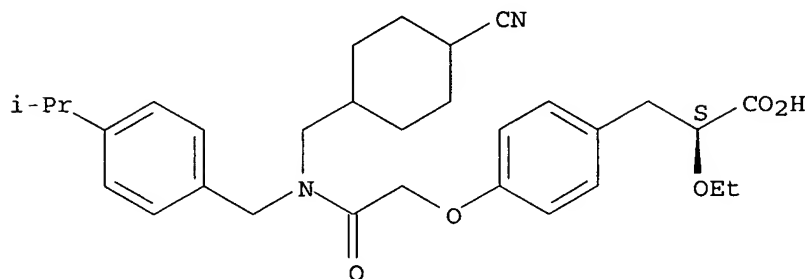
Absolute stereochemistry.



RN 817181-63-8 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[[(4-cyanocyclohexyl)methyl][4-(1-methylethyl)phenyl]methyl]amino]-2-oxoethoxy]-α-ethoxy-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



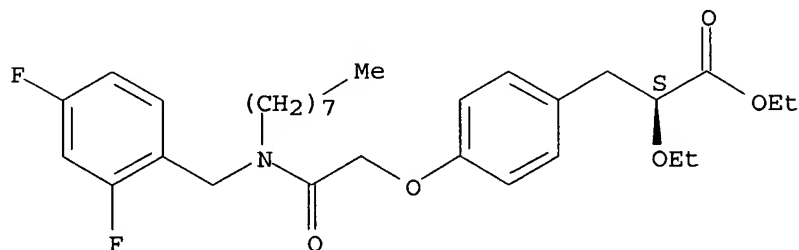
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816465-46-0P 816465-49-3P 816465-52-8P  
816465-56-2P 816465-58-4P

(preparation of phenylpropanoic acid derivs. as PPARα agonists)

RN 816465-06-2 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[[(2,4-difluorophenyl)methyl]octylamino]-2-oxoethoxy]-α-ethoxy-, ethyl ester, (αS)- (9CI) (CA INDEX NAME)

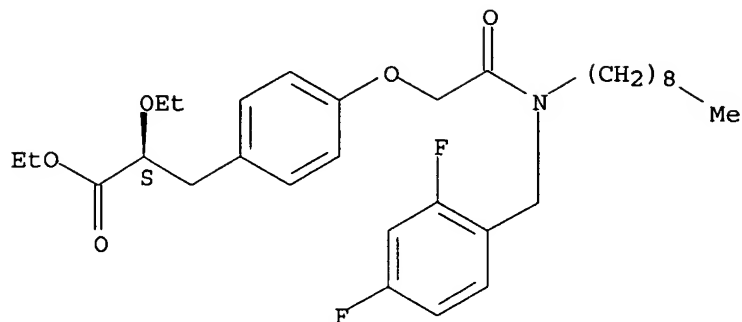
Absolute stereochemistry.



RN 816465-10-8 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[[(2,4-difluorophenyl)methyl]nonylaminol]-2-oxoethoxy]-α-ethoxy-, ethyl ester, (αS)- (9CI) (CA INDEX NAME)

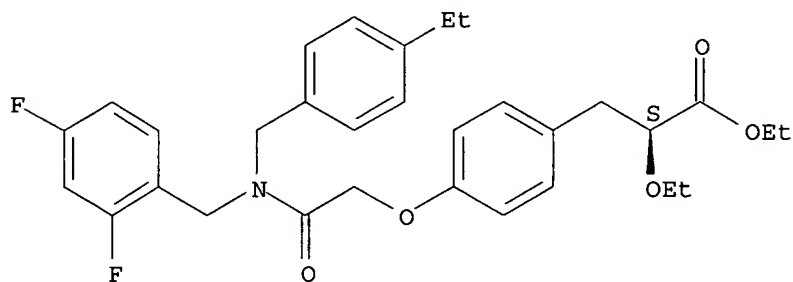
Absolute stereochemistry.



RN 816465-14-2 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[[(2,4-difluorophenyl)methyl][(4-ethylphenyl)methyl]amino]-2-oxoethoxy]- $\alpha$ -ethoxy-, ethyl ester, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

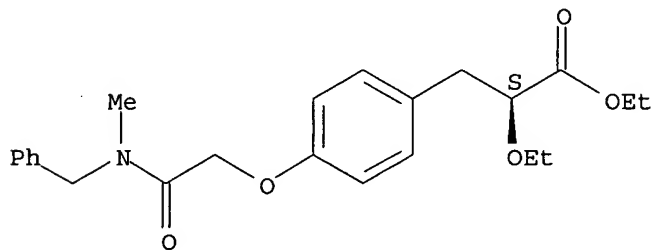
Absolute stereochemistry.



RN 816465-16-4 HCAPLUS

CN Benzenepropanoic acid,  $\alpha$ -ethoxy-4-[2-[methyl(phenylmethyl)amino]-2-oxoethoxy]-, ethyl ester, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

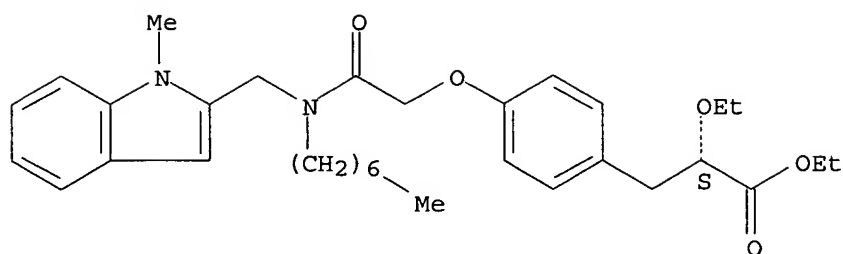
Absolute stereochemistry.



RN 816465-19-7 HCAPLUS

CN Benzenepropanoic acid,  $\alpha$ -ethoxy-4-[2-[heptyl[(1-methyl-1H-indol-2-yl)methyl]amino]-2-oxoethoxy]-, ethyl ester, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

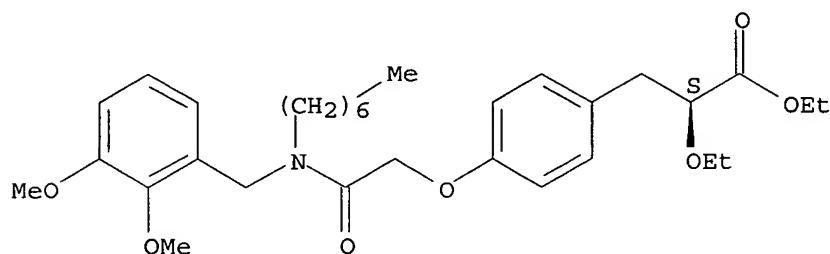
Absolute stereochemistry.



RN 816465-22-2 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[[(2,3-dimethoxyphenyl)methyl]heptylamino]-2-oxoethoxy]-α-ethoxy-, ethyl ester, (αS)- (9CI)  
(CA INDEX NAME)

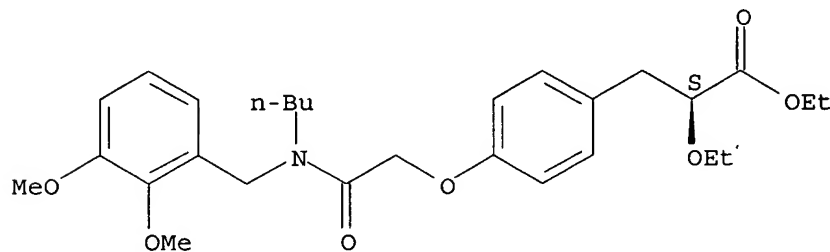
Absolute stereochemistry.



RN 816465-24-4 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[butyl[(2,3-dimethoxyphenyl)methyl]amino]-2-oxoethoxy]-α-ethoxy-, ethyl ester, (αS)- (9CI) (CA INDEX NAME)

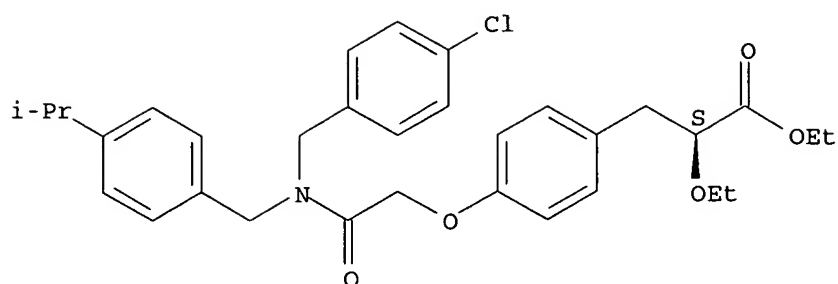
Absolute stereochemistry.



RN 816465-27-7 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[[(4-chlorophenyl)methyl][4-(1-methylethyl)phenyl]methyl]amino]-2-oxoethoxy]-α-ethoxy-, ethyl ester, (αS)- (9CI) (CA INDEX NAME)

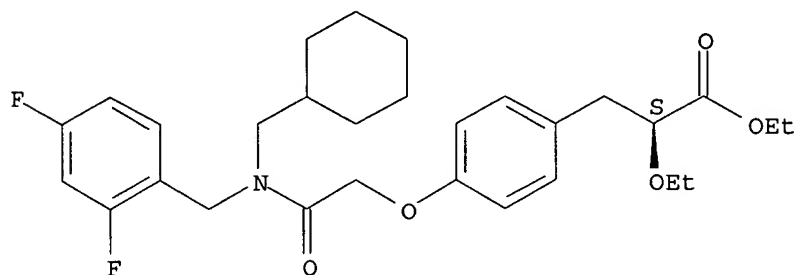
Absolute stereochemistry.



RN 816465-31-3 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[(cyclohexylmethyl)[(2,4-difluorophenyl)methyl]amino]-2-oxoethoxy]- $\alpha$ -ethoxy-, ethyl ester, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

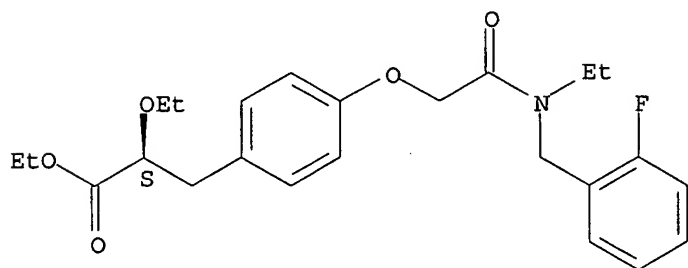
Absolute stereochemistry.



RN 816465-34-6 HCAPLUS

CN Benzenepropanoic acid,  $\alpha$ -ethoxy-4-[2-[ethyl[(2-fluorophenyl)methyl]amino]-2-oxoethoxy]-, ethyl ester, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

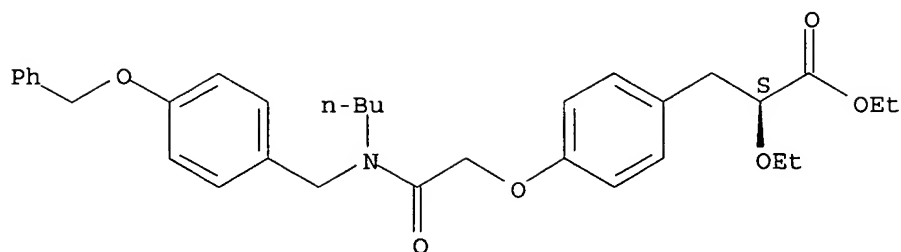
Absolute stereochemistry.



RN 816465-36-8 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[butyl[[4-(phenylmethoxy)phenyl]methyl]amino]-2-oxoethoxy]- $\alpha$ -ethoxy-, ethyl ester, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

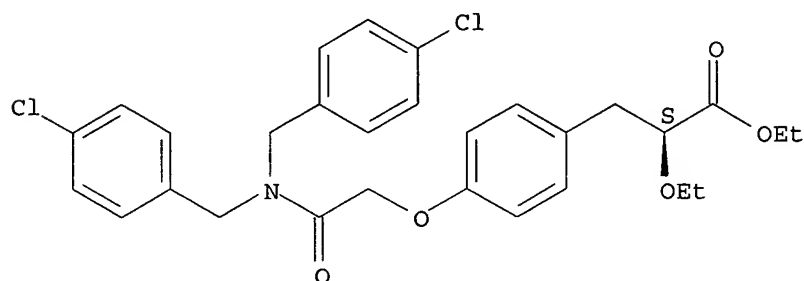
Absolute stereochemistry.



RN 816465-39-1 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[bis[(4-chlorophenyl)methyl]amino]-2-oxoethoxy]- $\alpha$ -ethoxy-, ethyl ester, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

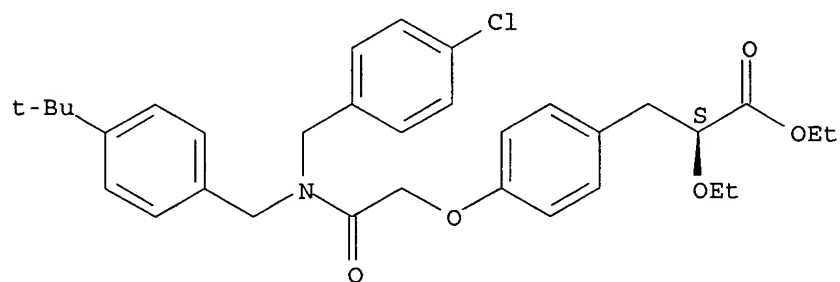
Absolute stereochemistry.



RN 816465-46-0 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[[(4-chlorophenyl)methyl][4-(1,1-dimethylethyl)phenyl]methyl]amino]-2-oxoethoxy]- $\alpha$ -ethoxy-, ethyl ester, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

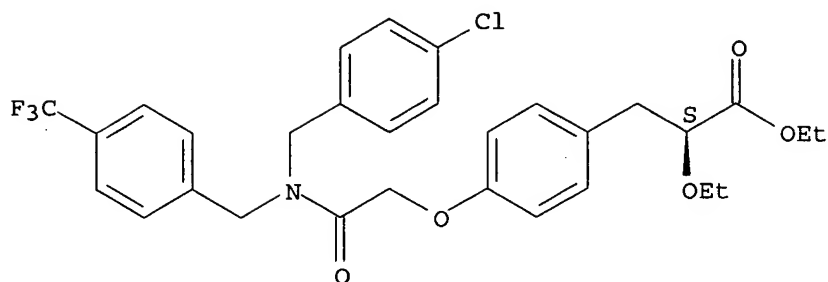


RN 816465-49-3 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[[(4-chlorophenyl)methyl][4-(trifluoromethyl)phenyl]methyl]amino]-2-oxoethoxy]- $\alpha$ -ethoxy-, ethyl ester, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

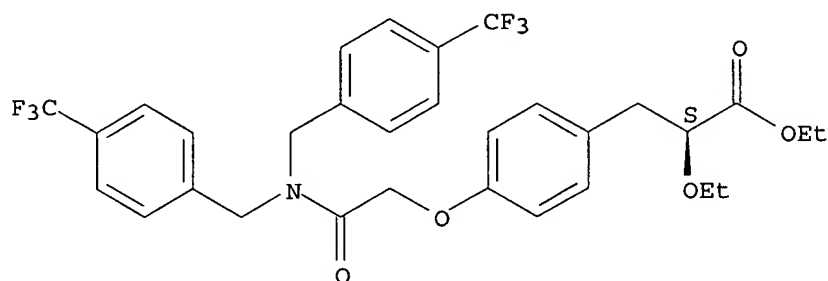




RN 816465-52-8 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[bis[[4-(trifluoromethyl)phenyl]methyl]amino]-2-oxoethoxy]-α-ethoxy-, ethyl ester, (αS)-(9CI) (CA INDEX NAME)

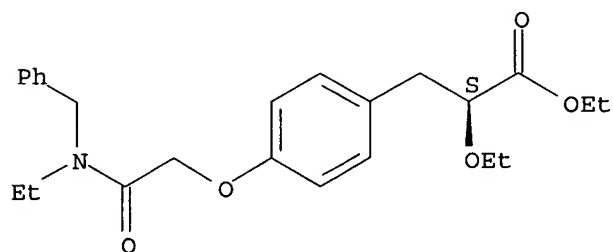
Absolute stereochemistry.



RN 816465-56-2 HCAPLUS

CN Benzenepropanoic acid, α-ethoxy-4-[2-[ethyl(phenylmethyl)amino]-2-oxoethoxy]-, ethyl ester, (αS)-(9CI) (CA INDEX NAME)

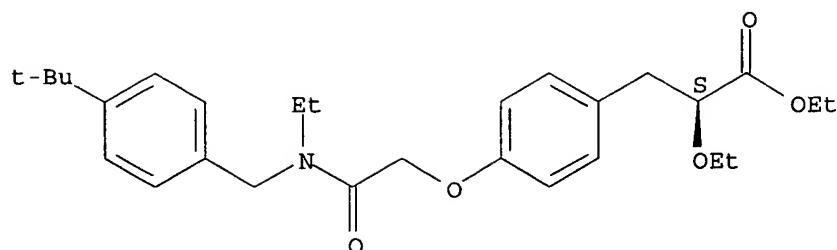
Absolute stereochemistry.



RN 816465-58-4 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[[4-(1,1-dimethylethyl)phenyl]methyl]ethylamino]-2-oxoethoxy]-α-ethoxy-, ethyl ester, (αS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



- IC ICM C07C231-00  
 CC 25-9 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)  
 Section cross-reference(s): 1, 63  
 ST phenylpropanoic acid prepn PPAR alpha agonist **antidiabetic**  
 IT **Diabetes mellitus**  
 (non-insulin-dependent; preparation of phenylpropanoic acid derivs.  
 as PPAR $\alpha$  agonists)  
 IT **Antidiabetic agents**  
 Antihypertensives  
 Antiobesity agents  
 Atherosclerosis  
 Drug delivery systems  
 Human  
 Hypertension  
 Obesity  
**Peroxisome proliferators**  
 (preparation of phenylpropanoic acid derivs. as PPAR $\alpha$   
 agonists)  
 IT **Peroxisome proliferator-activated receptors**  
 ( $\alpha$ ; preparation of phenylpropanoic acid derivs. as PPAR $\alpha$   
 agonists)  
 IT **Peroxisome proliferator-activated receptors**  
 ( $\gamma$ ; preparation of phenylpropanoic acid derivs. as PPAR $\alpha$   
 agonists)  
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 817181-63-8P

(preparation of phenylpropanoic acid derivs. as PPAR $\alpha$  agonists)

IT 114413-73-9P, N-Butyl-N-(2,3-dimethoxybenzyl)amine 500789-57-1P,  
 N-Butyl-2,3-dimethoxybenzamide 637015-19-1P,  
 N-(2,3-Dimethoxybenzyl)-N-heptylamine 816465-04-0P,  
 N-(2,4-Difluorobenzyl)octanamide 816465-05-1P  
 816465-06-2P 816465-08-4P, N-(2,4-Difluorobenzyl)nonanamide 816465-09-5P 816465-10-8P  
 816465-12-0P, N-(2,4-Difluorobenzyl)-4-ethylbenzamide  
 816465-13-1P 816465-14-2P 816465-16-4P  
 816465-18-6P 816465-19-7P 816465-21-1P,  
 N-Heptyl-2,3-dimethoxybenzamide 816465-22-2P  
 816465-24-4P 816465-26-6P 816465-27-7P  
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 816465-46-0P 816465-49-3P 816465-52-8P  
 816465-56-2P 816465-58-4P

(preparation of phenylpropanoic acid derivs. as PPAR $\alpha$  agonists)

L32 ANSWER 3 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:546469 HCAPLUS

DOCUMENT NUMBER: 141:106266

TITLE: Preparation of phenylpropanoic acids  
 derivatives as selective PPAR $\alpha$   
 modulators

INVENTOR(S): Lindstedt Alstermark, Eva-Lotte; Olsson, Anna  
 Christina; Li, Lanna; Aurell, Carl-Johan;  
 Minidis, Anna; Yousefi-Salakdeh, Esmail;  
 Dahlstrom, Mikael Ulf Johan

PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited

SOURCE: PCT Int. Appl., 43 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 5

## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004056748	A1	20040708	WO 2003-GB5602	2003 1219
<p>W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW</p> <p>RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG</p>				
CA 2508851	AA	20040708	CA 2003-2508851	2003 1219
AU 2003290309	A1	20040714	AU 2003-290309	2003 1219
US 2005131068	A1	20050616	US 2003-499893	2003 1219
EP 1572626	A1	20050914	EP 2003-782668	2003 1219
BR 2003017458	A	20051116	BR 2003-17458	2003 1219
CN 1753862	A	20060329	CN 2003-80109895	2003 1219
JP 2006511572	T2	20060406	JP 2004-561668	2003 1219
JP 3786945	B2	20060621		
US 2005282822	A1	20051222	US 2004-26806	2004 1230
NO 2005002914	A	20050719	NO 2005-2914	2005 0615

JP 2006045240

A2

20060216

JP 2005-253346

2005  
0901

## PRIORITY APPLN. INFO.:

GB 2002-29931

A

2002  
1221

SE 2001-4334

A

2001  
1219

WO 2002-GB5738

W

2002  
1218

WO 2002-GB5744

A

2002  
1218

GB 2003-14079

A

2003  
0618

JP 2004-561668

A3

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WO 2003-GB305602

A

2003  
1219

WO 2003-GB5602

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2003  
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WO 2004-EP6597

A

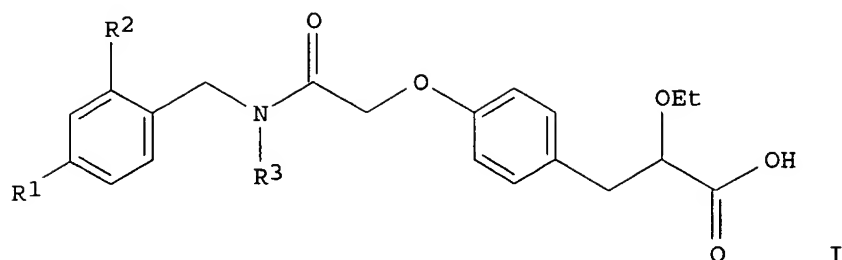
2004  
0617

US 2005-499261

A2

2005  
0304OTHER SOURCE(S):  
GI

CASREACT 141:106266; MARPAT 141:106266



AB Title compds. I [R1 = Cl, CF3, CF3O; R2 = H, F; R3 = alkyl] and their pharmaceutically acceptable salts, prodrugs were prepared For example, amidation of N-butyl-N-[2-fluoro-4-(trifluoromethyl)benzyl]amine, e.g., prepared from Et (2S)-2-ethoxy-3-(4-hydroxyphenyl)propanoate in 3 steps, and {4-[(2S)-2,3-diethoxy-3-oxopropyl]phenoxy}acetic acid, followed by hydrolysis afforded compound (S)-I [R1 = CF3; R2 = F; R3 = butyl] in 72% yield. Compds. I have EC50 values <0.1  $\mu\text{mol/L}$  for PPAR $\alpha$ , e.g., the EC50 value of compound (S)-I [R1 = CF3; R2 = F; R3 = butyl] was 0.001  $\mu\text{mol/L}$ . Of notes, compds. I exhibit improved metabolic stability (in vitro), promising toxicol. profile (no data provided) and particular compds. have the ratio of the EC50(PPAR $\gamma$ ):EC50(PPAR $\gamma$ ) <150:1. Compds. I are claimed useful for the treatment of hypertension, **diabetes**, etc.

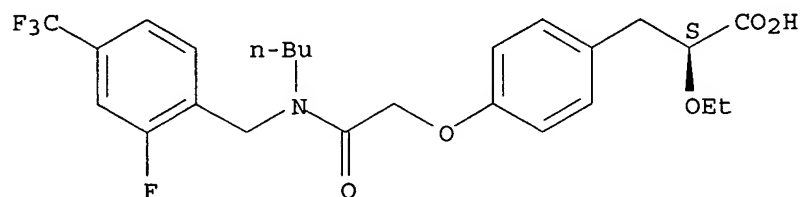
IT 719277-13-1P 719277-14-2P 719277-15-3P  
719277-16-4P 719277-17-5P

(preparation of phenylpropanoic acids derivs. as selective PPAR $\alpha$  modulators for treatment of dyslipidemia)

RN 719277-13-1 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[butyl[(2-fluoro-4-(trifluoromethyl)phenyl)methyl]amino]-2-oxoethoxy]- $\alpha$ -ethoxy-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

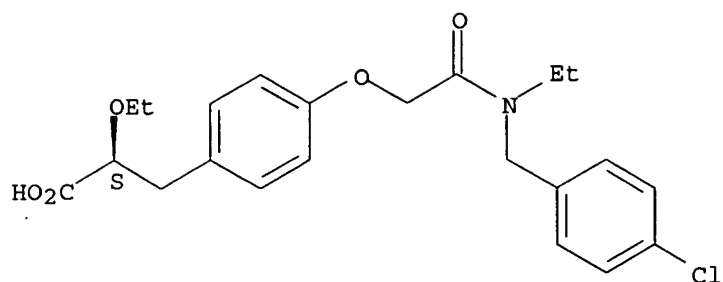
Absolute stereochemistry.



RN 719277-14-2 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[[4-chlorophenyl)methyl]ethylamino]-2-oxoethoxy]- $\alpha$ -ethoxy-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

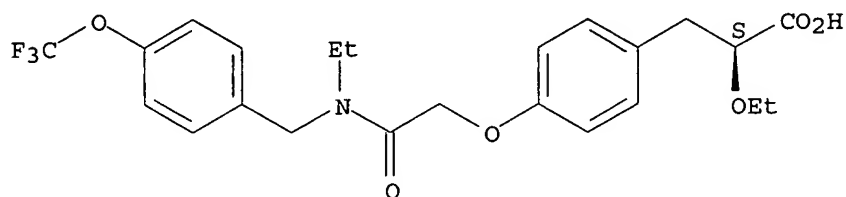
Absolute stereochemistry.



RN 719277-15-3 HCAPLUS

CN Benzenepropanoic acid,  $\alpha$ -ethoxy-4-[2-[ethyl[[4-(trifluoromethoxy)phenyl]methyl]amino]-2-oxoethoxy]-, ( $\alpha$ S)-(9CI) (CA INDEX NAME)

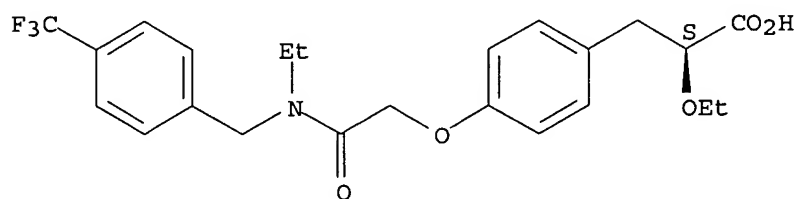
Absolute stereochemistry.



RN 719277-16-4 HCAPLUS

CN Benzenepropanoic acid,  $\alpha$ -ethoxy-4-[2-[ethyl[[4-(trifluoromethyl)phenyl]methyl]amino]-2-oxoethoxy]-, ( $\alpha$ S)-(9CI) (CA INDEX NAME)

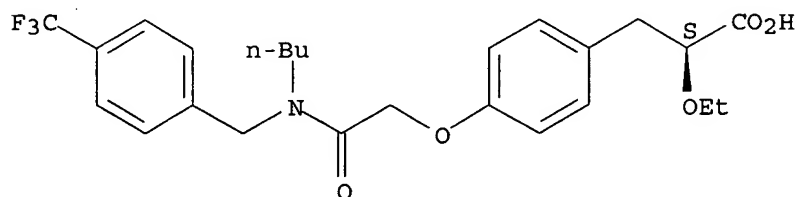
Absolute stereochemistry.



RN 719277-17-5 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[butyl[[4-(trifluoromethyl)phenyl]methyl]amino]-2-oxoethoxy]- $\alpha$ -ethoxy-, ( $\alpha$ S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



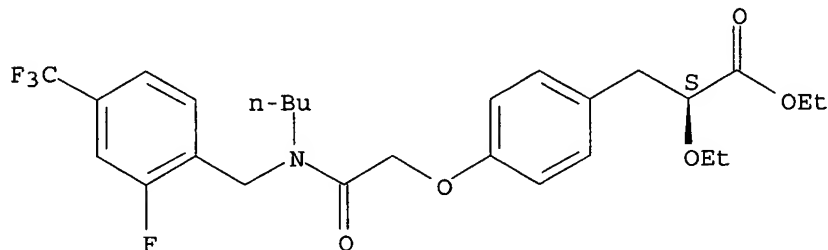
IT 719277-19-7P 719277-20-0P 719277-23-3P  
719277-24-4P 765303-27-3P

(preparation of phenylpropanoic acids derivs. as selective  
PPAR $\alpha$  modulators for treatment of dyslipidemia)

RN 719277-19-7 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[butyl[[2-fluoro-4-(trifluoromethyl)phenyl]methyl]amino]-2-oxoethoxy]- $\alpha$ -ethoxy-, ethyl ester, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

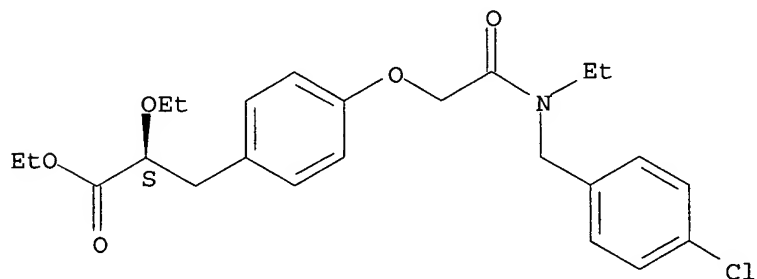
Absolute stereochemistry.



RN 719277-20-0 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[[(4-chlorophenyl)methyl]ethylamino]-2-oxoethoxy]- $\alpha$ -ethoxy-, ethyl ester, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

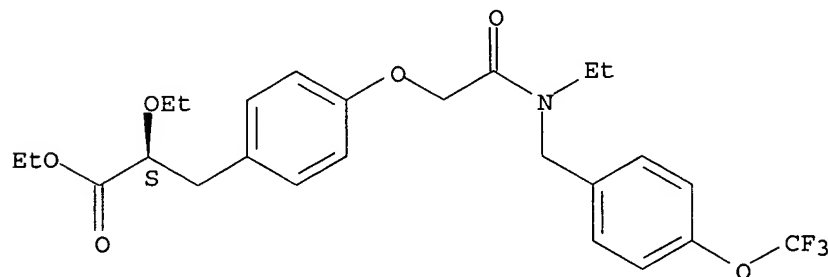
Absolute stereochemistry.



RN 719277-23-3 HCAPLUS

CN Benzenepropanoic acid,  $\alpha$ -ethoxy-4-[2-[ethyl[[4-(trifluoromethoxy)phenyl]methyl]amino]-2-oxoethoxy]-, ethyl ester, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

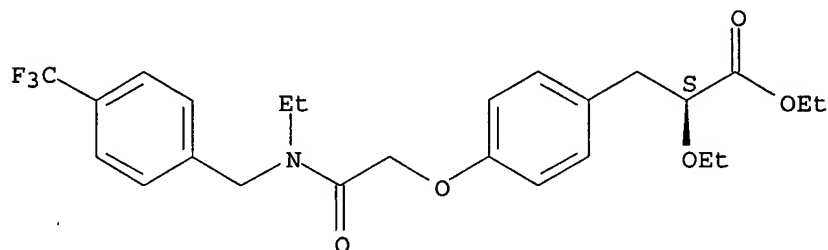
Absolute stereochemistry.





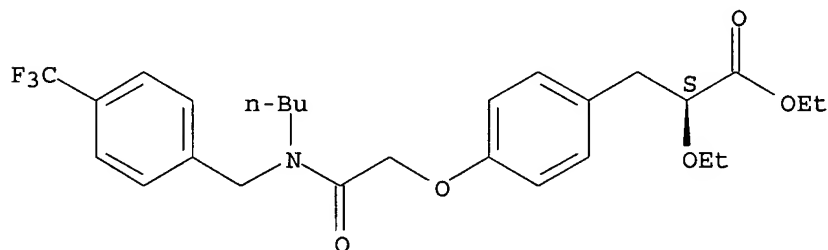
RN 719277-24-4 HCAPLUS  
 CN Benzenepropanoic acid,  $\alpha$ -ethoxy-4-[2-[ethyl[[4-(trifluoromethyl)phenyl]methyl]amino]-2-oxoethoxy]-, ethyl ester, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 765303-27-3 HCAPLUS  
 CN Benzenepropanoic acid, 4-[2-[butyl[[4-(trifluoromethyl)phenyl]methyl]amino]-2-oxoethoxy]- $\alpha$ -ethoxy-, ethyl ester, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IC ICM C07C235-20  
 ICS A61K031-16  
 CC 25-17 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)  
 Section cross-reference(s): 1, 63  
 ST phenylpropanoic acid prepn PPAR alpha modulator prodrug; antihypertensive phenylpropanoic acid prepn PPAR alpha modulator prodrug; antidiabetic agent phenylpropanoic acid prepn PPAR alpha modulator prodrug  
 IT **Peroxisome proliferators**  
 (medicaments with; preparation of phenylpropanoic acids derivs. as selective PPAR $\alpha$  modulators for treatment of dyslipidemia)  
 IT **Antidiabetic agents**  
 Antihypertensives  
 Antiobesity agents  
 Drug delivery systems  
 Human  
 (preparation of phenylpropanoic acids derivs. as selective PPAR $\alpha$  modulators for treatment of dyslipidemia)  
 IT **Peroxisome proliferator-activated receptors**  
 (preparation of phenylpropanoic acids derivs. as selective PPAR $\alpha$  modulators for treatment of dyslipidemia)  
 IT Atherosclerosis

Diabetes mellitus  
Hypertension  
Obesity

(treatment of; preparation of phenylpropanoic acids derivs. as selective PPAR $\alpha$  modulators for treatment of dyslipidemia)

IT 719277-13-1P 719277-14-2P 719277-15-3P

719277-16-4P 719277-17-5P

(preparation of phenylpropanoic acids derivs. as selective PPAR $\alpha$  modulators for treatment of dyslipidemia)

IT 549501-67-9P 549501-68-0P 719277-18-6P 719277-19-7P

719277-20-0P 719277-21-1P 719277-22-2P

719277-23-3P 719277-24-4P 765303-27-3P

(preparation of phenylpropanoic acids derivs. as selective PPAR $\alpha$  modulators for treatment of dyslipidemia)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE  
FOR THIS RECORD. ALL CITATIONS AVAILABLE  
IN THE RE FORMAT

L32 ANSWER 4 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:412940 HCAPLUS

DOCUMENT NUMBER: 141:7105

TITLE: Preparation of thienyl- and thiazolecarboxamides as inhibitors of ROCK, ERK, GSK, and AGC protein kinases

INVENTOR(S): Cao, Jingrong; Gao, Huai; Green, Jeremy; Marhefka, Craig

PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA

SOURCE: PCT Int. Appl., 222 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004041813	A1	20040521	WO 2003-US34319	2003 1030

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RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2504320 AA 20040521 CA 2003-2504320

2003  
1030

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AU 2003288956 A1 20040607 AU 2003-288956

2003  
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US 2004122016 A1 20040624 US 2003-696862  
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EP 1558607 A1 20050803 EP 2003-781448  
2003  
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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,  
MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ,  
EE, HU, SK  
CN 1732164 A 20060208 CN 2003-80108111  
2003  
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JP 2006514684 T2 20060511 JP 2005-502202  
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NO 2005002595 A 20050627 NO 2005-2595  
2005  
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PRIORITY APPLN. INFO.: US 2002-422441P P  
2002  
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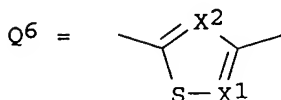
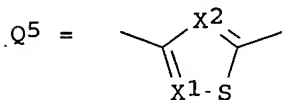
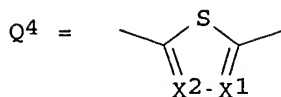
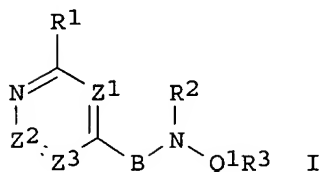
US 2003-476433P P  
2003  
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US 2003-476691P P  
2003  
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US 2003-479903P P  
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WO 2003-US34319 W  
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OTHER SOURCE(S): MARPAT 141:7105  
GI

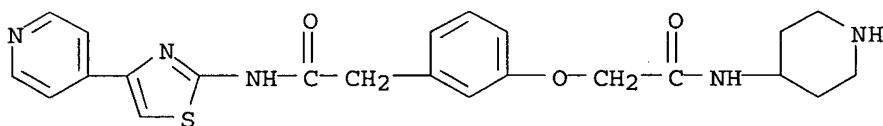


AB Title compds. [I; B = Q4, Q5, Q6; R1 = halo, cyano, NO<sub>2</sub>, VmR; Z1, Z3 = N, CRz; Z2 = N, CR1; Rz = halo, cyano, NO<sub>2</sub>, UnR'; R2 = UnR'; X1, X2 = CR4, N; R4 = halo, cyano, NO<sub>2</sub>, VmR; U, V = (substituted) alkylidene optionally interrupted by NR, O, S, CS, SO, SO<sub>2</sub>, CO<sub>2</sub>, etc.; m, n = 0, 1; R = H, (substituted) aliphatic; R' = R, (unsatd.) (heterocyclic) mono- or bicyclic ring; Q1 = CO, SO<sub>2</sub>, CONR, SO<sub>2</sub>NR; R3 = Q2Ar1; R2Q1R3 = atoms to form a cyclic group; Ar1 = (unsatd.) (heterocyclic) mono- or bicyclic ring; with provisos], were prepared Thus, 2-chloro-N-(4-pyridin-4-ylthiazol-2-yl)acetamide and N-methylaniline were stirred overnight in DMF at 70° to give 2-(methylphenylamino)-N-(4-pyridin-4-ylthiazol-2-yl)acetamide. Certain I were shown to inhibit ROCK I, ERK2, GSK3, and PKA with K<sub>i</sub> <1 μM.

IT 692885-81-7P 692885-86-2P  
(claimed compound; preparation of thiophene- and thiazolecarboxamides as inhibitors of ROCK, ERK, GSK, and AGC protein kinases)

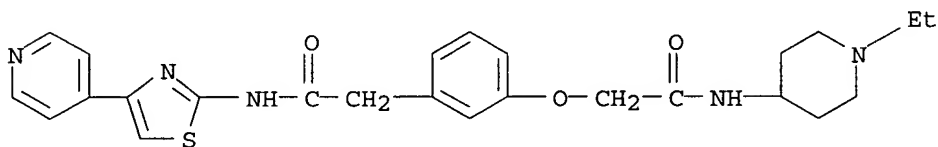
RN 692885-81-7 HCAPLUS

CN Benzeneacetamide, 3-[2-oxo-2-(4-piperidinylamino)ethoxy]-N-[4-(4-pyridinyl)-2-thiazolyl]- (9CI) (CA INDEX NAME)



RN 692885-86-2 HCAPLUS

CN Benzeneacetamide, 3-[2-[(1-ethyl-4-piperidinyl)amino]-2-oxoethoxy]-N-[4-(4-pyridinyl)-2-thiazolyl]- (9CI) (CA INDEX NAME)



IC ICM C07D409-04  
ICS C07D417-04; C07D417-14; C07D409-14

CC 28-7 (Heterocyclic Compounds (More Than One Hetero Atom))  
Section cross-reference(s): 1, 27, 63

IT Allergy inhibitors  
Anti-AIDS agents  
Anti-inflammatory agents  
Antianginal agents  
Antiarteriosclerotics  
Antiasthmatics  
Antidiabetic agents  
Antihypertensives  
Antipsychotics  
Antitumor agents  
Antiviral agents  
Cardiovascular agents  
Cytotoxic agents  
Drug delivery systems

Human

Nervous system agents

(preparation of thiophene- and thiazolecarboxamides as inhibitors of  
ROCK, ERK, GSK, and AGC protein kinases)

IT AIDS (disease)

Allergy

Alopecia

Arteriosclerosis

Asthma

Atherosclerosis

Autoimmune disease

Bone, disease

Cystic fibrosis

Diabetes mellitus

Heart, disease

Hypertension

Immune disease

Inflammation

Ischemia

Multiple sclerosis

Neoplasm

Osteoporosis

Psoriasis

Schizophrenia

(treatment; preparation of thiophene- and thiazolecarboxamides as  
inhibitors of ROCK, ERK, GSK, and AGC protein kinases)

IT	692878-12-9P	692878-18-5P	692878-23-2P	692878-28-7P
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692887-81-3P 692887-87-9P 692887-92-6P 692887-96-0P  
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692888-66-7P 692888-72-5P 692888-76-9P 692891-91-1P  
693025-22-8P

(claimed compound; preparation of thiophene- and thiazolecarboxamides  
as inhibitors of ROCK, ERK, GSK, and AGC protein kinases)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE  
FOR THIS RECORD. ALL CITATIONS AVAILABLE  
IN THE RE FORMAT

L32 ANSWER 5 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:392321 HCAPLUS

DOCUMENT NUMBER: 140:406826

TITLE: Preparation of N-benzylpiperazine derivatives  
as chemokine receptor CCR1 antagonists useful  
as immunomodulatory agents

INVENTOR(S): Blumberg, Laura C.; Brown, Matthew F.; Gaweco,  
Anderson S.; Gladue, Ronald P.; Hayward,  
Matthew M.; Lundquist, Gregory D.; Poss,  
Christopher S.; Shavnya, Andrei

PATENT ASSIGNEE(S): Pfizer Inc, USA

SOURCE: U.S. Pat. Appl. Publ., 58 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

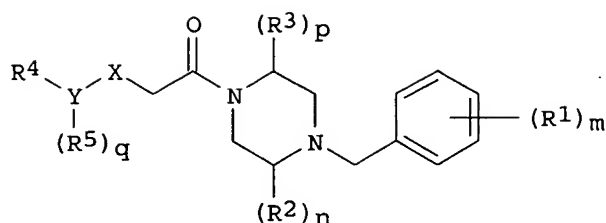
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004092529	A1	20040513	US 2003-686993	2003 1016

PRIORITY APPLN. INFO.: US 2002-422590P P 2002  
1030

OTHER SOURCE(S): MARPAT 140:406826  
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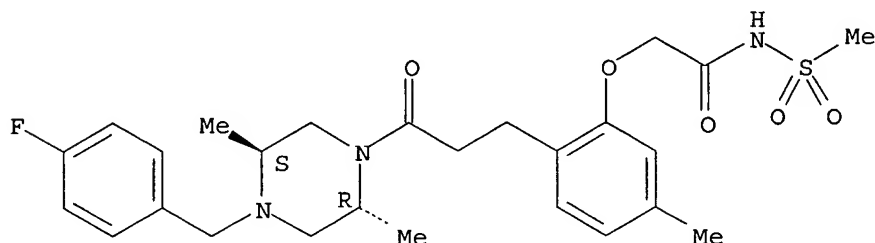
AB The present invention relates to compds. of the formula (I) and the pharmaceutically acceptable forms thereof [m = 0-5; n, p = 0-2; q = 0-4; X = O, S, CH<sub>2</sub>, (un)substituted NH; Y = C<sub>6</sub>-10 aryl, C<sub>2</sub>-9 heteroaryl; R<sub>1</sub> = H, HO, halo, C<sub>1</sub>-8 alkyl, C<sub>1</sub>-8 alkoxy, HO-C<sub>1</sub>-8 alkyl, cyano, NH<sub>2</sub>, H<sub>2</sub>N-C<sub>1</sub>-8 alkyl, CO<sub>2</sub>H, C<sub>1</sub>-8 alkyl-CO, C<sub>1</sub>-8 alkyl-CO-C<sub>1</sub>-8 alkyl, CONH<sub>2</sub>, or H<sub>2</sub>NCO-C<sub>1</sub>-8 alkyl; R<sub>2</sub>, R<sub>3</sub> = H, oxo, C<sub>1</sub>-8 alkyl, C<sub>3</sub>-8 cycloalkyl-C<sub>1</sub>-8 alkyl, C<sub>6</sub>-10 aryl, C<sub>6</sub>-10 aryl-C<sub>1</sub>-8 alkyl, HO-C<sub>1</sub>-8 alkyl, C<sub>1</sub>-8 alkyl-O-C<sub>1</sub>-8 alkyl, H<sub>2</sub>N-C<sub>1</sub>-8 alkyl, C<sub>1</sub>-8 alkyl-NH-C<sub>1</sub>-8 alkyl, (C<sub>1</sub>-8 alkyl)<sub>2</sub>N-C<sub>1</sub>-8 alkyl, C<sub>2</sub>-9 heterocyclyl-C<sub>1</sub>-8 alkyl, C<sub>3</sub>-8 cycloalkyl-NH-C<sub>1</sub>-8 alkyl, C<sub>1</sub>-8 alkyl-CO-NH-C<sub>1</sub>-8 alkyl, C<sub>1</sub>-8 alkyl-O-CO-NH-C<sub>1</sub>-8 alkyl, H<sub>2</sub>NCO-NH-C<sub>1</sub>-8 alkyl, C<sub>1</sub>-8 alkyl-SO<sub>2</sub>NH-C<sub>1</sub>-8 alkyl, C<sub>2</sub>-9 heteroaryl-C<sub>1</sub>-8 alkyl, H<sub>2</sub>NCO, H<sub>2</sub>NCO-C<sub>1</sub>-8 alkyl; R<sub>4</sub> = (HO<sub>2</sub>C)(H<sub>2</sub>N)-C<sub>1</sub>-8 alkyl, (HO<sub>2</sub>C)[(C<sub>1</sub>-8 alkyl)NH]-C<sub>1</sub>-8 alkyl, (HO<sub>2</sub>C)[(C<sub>1</sub>-8 alkyl)<sub>2</sub>N]-C<sub>1</sub>-8 alkyl, (HO<sub>2</sub>C-C<sub>1</sub>-8 alkyl)(C<sub>1</sub>-8 alkyl)N, (HO<sub>2</sub>C-C<sub>1</sub>-8 alkyl)(C<sub>1</sub>-8 alkyl)N-C<sub>1</sub>-8 alkyl, (HO<sub>2</sub>C-C<sub>1</sub>-8 alkyl)(C<sub>1</sub>-8 alkyl-SO<sub>2</sub>)N, (HO<sub>2</sub>C-C<sub>1</sub>-8 alkyl)(C<sub>1</sub>-8 alkyl-SO<sub>2</sub>)N-C<sub>1</sub>-8 alkyl, (HO<sub>2</sub>C-C<sub>1</sub>-8 alkyl)(C<sub>1</sub>-8 alkyl-CO)N, etc.; R<sub>5</sub> = H, HO, halo, cyano, CO<sub>2</sub>H, H<sub>2</sub>N, C<sub>1</sub>-8 alkyl-NH, (C<sub>1</sub>-8 alkyl)<sub>2</sub>N, C<sub>1</sub>-8 alkyl, C<sub>1</sub>-8 alkyl-O, HO-C<sub>1</sub>-8 alkyl, C<sub>1</sub>-8 alkyl-NH-C<sub>1</sub>-8 alkyl, (C<sub>1</sub>-8 alkyl)<sub>2</sub>N-C<sub>1</sub>-8 alkyl, etc.]. Moreover, the present invention is also directed at pharmaceutical compns. comprising the compound I and a pharmaceutically acceptable carrier. Furthermore, the present invention is directed at methods of using the herein described compds. and compns. for treating or preventing a disorder or condition that can be treated or prevented by antagonizing the CCR1 receptor in a mammal. Particularly, disclosed is a method of treating or preventing a disorder or condition selected from the group consisting of fibrosis, Alzheimer's disease, conditions associated with leptin production, sequelae associated with cancer, cancer metastasis, diseases or conditions related to production of cytokines at inflammatory sites, and tissue damage caused by inflammation induced by infectious agents, wherein the method comprises administering to a mammal in need of such treatment or prevention a pharmaceutically effective amount of the compound I or a pharmaceutically acceptable form thereof. The compds. I are potent and selective inhibitors of MIP-1 $\alpha$  (CCL3) binding to its receptor CCR1 found on inflammatory and immunomodulatory cells (preferably leukocytes and lymphocytes). [2-[3-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-3-oxopropyl]-5-methylphenoxy]acetic acid was condensed with methanesulfonamide in CH<sub>2</sub>Cl<sub>2</sub> at room temperature for 18 h using 4-dimethylaminopyridine and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride to give N-[[2-[3-[4-(4-fluoro-benzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-3-oxo-propyl]-5-methylphenoxy]acetyl]methanesulfonamide. All the compds. I inhibited MIP-1 $\alpha$  (and the related chemokines shown to interact with CCR1) induced chemotaxis of THP-1 cells and human leukocytes with IC<sub>50</sub> of <10  $\mu$ M.

IT 519171-77-8P, N-[[2-[3-[4-(4-Fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-3-oxopropyl]-5-methylphenoxy]acetyl]methanesulfonamide 519173-15-0P, N-[[2-[3-[4-(4-Fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-3-oxopropyl]-5-methoxyphenoxy]acetyl]methanesulfonamide (preparation of N-benzylpiperazine derivs. as chemokine receptor CCR1 antagonists useful as immunomodulatory agents)

RN 519171-77-8 HCAPLUS

CN Acetamide, 2-[2-[3-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-3-oxopropyl]-5-methylphenoxy]-N-(methylsulfonyl)- (9CI) (CA INDEX NAME)

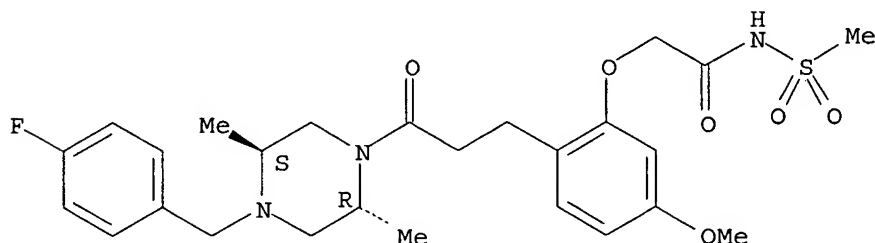
Absolute stereochemistry.



RN 519173-15-0 HCAPLUS

CN Acetamide, 2-[2-[3-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-3-oxopropyl]-5-methoxyphenoxy]-N-(methylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IC ICM A61K031-495

INCL 514255010

CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))  
Section cross-reference(s): 1

IT **Diabetes** mellitus  
(non-insulin-dependent; preparation of N-benzylpiperazine derivs. as chemokine receptor CCR1 antagonists useful as immunomodulatory agents)

IT Adenoviridae  
Alzheimer's disease  
Anorexia  
Anti-Alzheimer's agents  
**Antidiabetic** agents  
Antimalarials  
Antiobesity agents  
Antitumor agents  
Antiviral agents



Bone resorption  
Cachexia  
Cytomegalovirus  
Fibrosis  
Fungicides  
Human herpesvirus  
Hyperplasia  
Immunomodulators  
Lyme disease  
Malaria  
Mammary gland, neoplasm  
Obesity

(preparation of N-benzylpiperazine derivs. as chemokine receptor  
CCR1 antagonists useful as immunomodulatory agents)

IT 519171-77-8P, N-[[2-[3-[4-(4-Fluorobenzyl)-(2R,5S)-2,5-  
dimethylpiperazin-1-yl]-3-oxopropyl]-5-  
methylphenoxy]acetyl]methanesulfonamide 519171-81-4P,  
N-[[5-Chloro-2-[2-[4-(4-fluoro-benzyl)-(2R,5S)-2,5-dimethyl-  
piperazin-1-yl]-2-oxo-ethoxy]-phenoxy]-acetyl]-methanesulfonamide  
hydrochloride 519171-92-7P, [5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-  
(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-  
Phenylsulfamoyl]-Acetic Acid 519171-96-1P, 1-[5-Chloro-2-[2-[4-  
(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-  
Ethoxy]-Benzyl]-3-(2-Methylbenzenesulfonyl)-Urea 519171-98-3P,  
(2-Methylbenzenesulfonyl)-Carbamic acid 5-Chloro-2-[2-[4-(4-Fluoro-  
Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Benzyl  
Ester 519171-99-4P, 2-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-  
(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-  
Benzylsulfamoyl]-Propionic Acid 519172-00-0P,  
N-[[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-  
Piperazin-1-yl]-2-Oxo-Ethoxy]-Benzyloxy]-Acetyl]-  
Methanesulfonamide 519172-04-4P, 1-Acetyl-3-[5-Chloro-2-[2-[4-(4-  
Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-  
Benzyl]Sulfamide 519172-06-6P, [5-Chloro-2-[2-[4-(4-Fluoro-  
Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-  
Benzylideneaminooxy]-Acetic Acid 519172-07-7P,  
N-[[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-  
Piperazin-1-yl]-2-Oxo-Ethoxy]-Phenyl]-Acetyl]-Methanesulfonamide  
519172-09-9P, N-[[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-  
dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Phenyl]-Acetyl]-Sulfamide  
519172-10-2P, N-[3-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-  
Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Phenyl]-Propionyl]-  
Methanesulfonamide 519172-14-6P, 3-[5-Chloro-2-[2-[4-(4-Fluoro-  
Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Phenyl]-  
Acrylic Acid 519172-16-8P, [5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-  
(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-  
Benzenesulfonylamino]-Acetic Acid hydrochloride 519172-20-4P,  
5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-  
1-yl]-2-Oxo-Ethoxy]-N-[(2-Propylamino)Carbonyl]-Benzenesulfonamide  
519172-21-5P, 5-Chloro-N-(2,2-Dimethyl-Propionyl)-2-[2-[4-(4-  
Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-  
Benzenesulfonamide 519172-22-6P, 5-Chloro-2-[2-[4-(4-Fluoro-  
Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-N-(2-  
Hydroxy-2-Methyl-Propionyl)-Benzenesulfonamide 519172-24-8P,  
N-Acetyl-1-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-  
Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Phenyl]-Methanesulfonamide  
519172-30-6P, 1-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-  
Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Phenyl]-N-(2-Hydroxy-2-  
Methyl-Propionyl)-Methanesulfonamide 519172-33-9P,  
N-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R)-2-Methyl-Piperazin-1-

yl]-2-Oxo-Ethoxy]-Pyridin-3-yl]-Succinamic Acid 519172-37-3P,  
 N-[[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-  
 Piperazin-1-yl]-2-Oxo-Ethoxy]-Pyridin-3-yl]-Acetyl]-  
 Methanesulfonamide 519172-45-3P, 3-[5-Chloro-2-[2-[4-(4-Fluoro-  
 Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Pyridin-  
 3-yl]-Propionic Acid 519172-49-7P, [[5-Chloro-2-[2-[4-(4-Fluoro-  
 Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethylamino]-  
 Pyridine-3-Carbonyl]-Amino]-Acetic Acid 519172-55-5P,  
 2-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-  
 Piperazin-1-yl]-2-Oxo-Ethoxy]-Phenylsulfanyl]-2-Methyl-Propionic  
 Acid 519172-59-9P, 2-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-  
 2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Benzenesulfonyl]-2-  
 Methyl-Propionic Acid 519172-62-4P, [5-Chloro-2-[2-[4-(4-Fluoro-  
 Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-  
 Phenylmethanesulfonyl]-Acetic Acid 519172-65-7P,  
 N-[3-[3-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-  
 yl]-2-Oxo-Ethoxy]-6-Methyl-Pyridin-2-yl]-Propionyl]-  
 Methanesulfonamide 519172-70-4P, 2-Amino-3-[5-Chloro-2-[2-[4-(4-  
 Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-  
 Phenyl]-Propionic Acid 519172-73-7P, [[5-Chloro-2-[2-[4-(4-  
 Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-  
 Benzyl]-Methyl-Amino]-Acetic Acid 519172-75-9P,  
 2-[4-Chloro-2-(2H-Tetrazol-5-ylmethoxy)-Phenoxy]-1-[4-(4-Fluoro-  
 Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-Ethanone  
 519172-77-1P, 2-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-  
 Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Phenoxy]-Nicotinic Acid  
 hydrochloride 519172-78-2P, [2-[2-[(2R)-2-Carbamoylmethyl-4-(4-  
 Fluoro-Benzyl)-Piperazin-1-yl]-2-Oxo-Ethoxy]-5-Chloro-Phenoxy]-  
 Acetic Acid 519172-86-2P, (4S)-4-[5-Chloro-2-[2-[4-(4-Fluoro-  
 Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-  
 Phenoxy]-1-Methyl-Pyrrolidine-(2S)-2-Carboxylic Acid  
 dihydrochloride 519172-87-3P, 1-[5-Chloro-2-[2-[4-(4-Fluoro-  
 Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Phenyl]-  
 N-(Methoxycarbonyl)-Methanesulfonamide 519172-88-4P,  
 6-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-  
 Piperazin-1-yl]-2-Oxo-Ethoxy]-Phenoxy-methyl]-Nicotinic Acid  
 519172-90-8P, 5-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-  
 Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Phenyl]-5-Oxo-Pentanoic  
 Acid 519172-94-2P, 5-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-  
 2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Phenyl]-Dihydro-Furan-2-  
 One 519172-97-5P, 4-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-  
 2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Pyridin-3-ylamino]-  
 Butyric Acid acetate 519173-03-6P, [5-Chloro-2-[2-[4-(4-Fluoro-  
 Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-Pyridin-  
 3-ylamino]-Acetic Acid acetate 519173-10-5P,  
 1-[5-Chloro-2-[2-[4-(4-Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-  
 Piperazin-1-yl]-2-Oxo-Ethoxy]-Phenyl]-2-(1H-Tetrazol-5-yl)-  
 Ethanone hydrochloride 519173-13-8P, 1-[5-Chloro-2-[2-[4-(4-  
 Fluoro-Benzyl)-(2R,5S)-2,5-Dimethyl-Piperazin-1-yl]-2-Oxo-Ethoxy]-  
 Phenyl]-3-(1H-Tetrazol-5-yl)-Propan-1-One hydrochloride  
 519173-14-9P, [2-[3-[4-(4-Fluorobenzyl)-(2R,5S)-2,5-  
 dimethylpiperazin-1-yl]-3-oxopropyl]-5-methoxyphenoxy]acetic acid  
 519173-15-0P, N-[[2-[3-[4-(4-Fluorobenzyl)-(2R,5S)-2,5-  
 dimethylpiperazin-1-yl]-3-oxopropyl]-5-  
 methoxyphenoxy]acetyl]methanesulfonamide 519173-16-1P,  
 [5-Chloro-2-[3-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-  
 yl]-3-oxopropyl]phenoxy]acetic acid 519173-17-2P,  
 [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-  
 yl]-2-oxoethoxy]phenyl]-oxoacetic acid 519173-18-3P,  
 [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-

oxoethoxy]phenoxy]acetic acid 519173-19-4P, N-[[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]acetyl]methanesulfonamide 519173-20-7P, [5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]acetic acid 519173-21-8P, [5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]acetic acid 519173-22-9P, [5-Chloro-2-[2-[(2R)-2-ethyl-4-(4-fluorobenzyl)piperazin-1-yl]-2-oxoethoxy]phenoxy]acetic acid 519173-23-0P, N-[[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]acetyl]methanesulfonamide 519173-24-1P, N-[[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]acetyl]methanesulfonamide 519173-25-2P, N-[[5-Chloro-2-[2-[(2R)-2-ethyl-4-(4-fluorobenzyl)piperazin-1-yl]-2-oxoethoxy]phenoxy]acetyl]methanesulfonamide 519173-26-3P, 2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]-2-methylpropionic acid 519173-27-4P, 4-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]butyric acid 519173-28-5P, 6-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]pyridine-2-carboxylic acid 519173-29-6P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]difluoroacetic acid 519173-30-9P, (2R)-2-Amino-4-[5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]butyric acid 519173-31-0P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]difluoroacetic acid 519173-32-1P, 4-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]butyric acid 519173-33-2P, 2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]-2-methylpropionic acid 519173-34-3P, (2S)-2-Amino-4-[5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]butyric acid 519173-35-4P, 2-[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]-2-methylpropionic acid 519173-36-5P, [5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]difluoroacetic acid 519173-37-6P, 2-[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]-2-methylpropionic acid 519173-38-7P, [5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]difluoroacetic acid 519173-39-8P, (2S)-2-Amino-4-[5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]butyric acid 519173-40-1P, (2S)-2-Amino-4-[5-bromo-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]butyric acid 519173-41-2P, 4-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]pyridine-2-carboxylic acid 519173-42-3P, N-[(2R)-2-Amino-4-[5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]butyryl]methanesulfonamide 519173-43-4P, 2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]methylthiazole-4-carboxylic acid 519173-44-5P, 3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]methylfuran-2-carboxylic acid 519173-45-6P, 5-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]methylfuran-2-carboxylic acid 519173-46-7P, 3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]methylthiophene-2-carboxylic acid 519173-47-8P, 2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-

dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy)methyl]furan-3-carboxylic acid 519173-48-9P, 5-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy)methyl]thiophene-2-carboxylic acid 519173-49-0P, 3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy)methyl]furan-2-carboxylic acid 519173-50-3P, 3-[5-Bromo-2-[2-[4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy)methyl]furan-2-carboxylic acid 519173-51-4P, 5-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]-5-(2-methoxyethyl)pyrimidine-2,4,6-trione 519173-53-6P, 5-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]-5-methylpyrimidine-2,4,6-trione 519173-55-8P, 5-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]-5-ethylpyrimidine-2,4,6-trione 519173-58-1P, (2R)-2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]propionic acid 519173-60-5P, (2S)-2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]propionic acid 519173-62-7P, (4S)-4-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]pyrrolidine-2-carboxylic acid 519173-63-8P, 3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]-2,2-dimethylpropionic acid 519173-65-0P, (4S)-4-[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]pyrrolidine-(2S)-2-carboxylic acid 519173-67-2P, (4S)-4-[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]pyrrolidine-(2S)-2-carboxylic acid 519173-69-4P, (4S)-4-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]pyrrolidine-(2S)-2-carboxylic acid 519173-70-7P, N-[(4S)-4-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]pyrrolidine-2-carbonyl]methanesulfonamide 519173-72-9P, [3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]ureido]acetic acid 519173-73-0P, 3-[3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]ureido]propionic acid 519173-74-1P, 3-[3-[4-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]ureido]propionic acid 519173-75-2P, [3-[4-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]ureido]acetic acid 519173-76-3P, 1-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]-3-(methylsulfonyl)urea 519173-77-4P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzylsulfamoyl]acetic acid 519173-78-5P, 1-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzyl]-3-(methylsulfonyl)urea 519173-79-6P, 1-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzyl]-3-(2-methylbenzoyl)sulfamide 519173-80-9P, [5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzylideneaminoxy]acetic acid 519173-81-0P, [1-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]ethylideneaminoxy]acetic acid 519173-82-1P, [1-[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]ethylideneaminoxy]acetic acid 519173-83-2P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-

1-yl]-2-oxoethoxy]phenyl]phenylmethyleaminoxy]acetic acid  
519173-84-3P, [2-[2-[4-(4-Fluorobenzyl)-(2R,5S)-2,5-  
dimethylpiperazin-1-yl]-2-oxoethoxy]-5-  
methylbenzylideneaminoxy]acetic acid 519173-85-4P,  
(2S)-2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-  
dimethylpiperazin-1-yl]-2-oxoethoxy]benzyloxy]propionic acid  
519173-86-5P, (2R)-2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-  
2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzyloxy]propionic acid  
519173-87-6P, 2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-  
dimethylpiperazin-1-yl]-2-oxoethoxy]benzyloxy]-2-methylpropionic  
acid 519173-88-7P, Methylsulfonylcarbamic acid  
5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-  
yl]-2-oxoethoxy]benzyl ester 519173-89-8P, N-[5-Chloro-2-[2-[4-  
(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-  
oxoethoxy]benzoyl]methanesulfonamide 519173-90-1P,  
N-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-  
2-oxoethoxy]benzoyl]methanesulfonamide 519173-91-2P,  
N-[[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-  
1-yl]-2-oxoethoxy]phenyl]acetyl]methanesulfonamide 519173-92-3P,  
N-[[5-Chloro-2-[2-[4-(4-fluorobenzyl)piperazin-1-yl]-2-  
oxoethoxy]phenyl]acetyl]methanesulfonamide 519173-93-4P,  
N-[[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-  
dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]-  
trifluoromethanesulfonamide 519173-94-5P 519173-95-6P,  
N-[[2-[2-[4-(4-Fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-  
oxoethoxy]-4-methoxyphenyl]acetyl]methanesulfonamide  
519173-96-7P 519173-97-8P, N-[[5-Chloro-2-[2-[4-(4-fluorobenzyl)-  
(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]-2-  
methylbenzenesulfonamide 519173-98-9P, Ethanesulfonic acid  
N-[[5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-  
dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]amide  
519173-99-0P, 3,5-Dimethylisoxazole-4-sulfonic acid  
N-[[5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-  
dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]amide  
519174-00-6P, N-[[5-Bromo-2-[2-[4-(4-fluorobenzyl)piperazin-1-yl]-  
2-oxoethoxy]phenyl]acetyl]methanesulfonamide 519174-01-7P,  
(R)-N-[[5-Chloro-2-[2-[4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-  
2-oxoethoxy]phenyl]acetyl]methanesulfonamide 519174-02-8P,  
(R)-N-[[5-Bromo-2-[2-[4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-2-  
oxoethoxy]phenyl]acetyl]methanesulfonamide 519174-03-9P,  
N-[[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-  
dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]-4-  
methoxybenzenesulfonamide 519174-04-0P, 2-Chloro-N-[[5-chloro-2-  
[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-  
oxoethoxy]phenyl]acetyl]benzenesulfonamide 519174-05-1P,  
N-[[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-  
dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]-2-  
fluorobenzenesulfonamide 519174-06-2P, N-[[5-Chloro-2-[2-[4-(4-  
fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-  
oxoethoxy]phenyl]acetyl]-4-methylbenzenesulfonamide  
519174-07-3P, Propane-2-sulfonic acid [[5-chloro-2-[2-[4-(4-  
fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-  
oxoethoxy]phenyl]acetyl]amide 519174-08-4P, Propane-1-sulfonic  
acid [[5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-  
dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]amide  
519174-10-8P, 2-[4-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-  
dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]-N-cyanoacetamide  
519174-11-9P, N-[[4-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-  
dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]methanesulfonami  
de 519174-12-0P, (R)-N-[[4-Chloro-2-[2-[4-(4-fluorobenzyl)-2-

methylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]methanesulfonamide  
 519174-13-1P, N-[[5-Chloro-2-[2-[4-(3,4-difluorobenzyl)-(2R,5S)-  
 2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]methanesulfo  
 namide 519174-14-2P, N-[[5-Chloro-2-[2-[4-(4-chlorobenzyl)-  
 (2R,5S)-2,5-dimethylpiperazin-1-yl]-2-  
 oxoethoxy]phenyl]acetyl]methanesulfonamide 519174-15-3P,  
 N-[[2-[2-[4-(4-Fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-  
 oxoethoxy]phenyl]acetyl]methanesulfonamide 519174-16-4P,  
 N-[[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-  
 dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]phenylmethanesul  
 fonamide 519174-17-5P, N-[3-[2-[2-[4-(4-Fluorobenzyl)-(2R,5S)-  
 2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]propionyl]methanesu  
 lfonamide 519174-18-6P, (R)-N-[[5-Chloro-2-[2-[4-(4-  
 chlorobenzyl)-2-methylpiperazin-1-yl]-2-  
 oxoethoxy]phenyl]acetyl]methanesulfonamide 519174-19-7P,  
 (R)-N-[[5-Chloro-2-[2-[4-(3,4-difluorobenzyl)-2-methylpiperazin-1-  
 yl]-2-oxoethoxy]phenyl]acetyl]methanesulfonamide 519174-20-0P,  
 (R)-N-[[5-Chloro-2-[2-[2-ethyl-4-(4-fluorobenzyl)piperazin-1-yl]-2-  
 oxoethoxy]phenyl]acetyl]methanesulfonamide 519174-21-1P,  
 (R)-N-[[5-Bromo-2-[2-[2-ethyl-4-(4-fluorobenzyl)piperazin-1-yl]-2-  
 oxoethoxy]phenyl]acetyl]methanesulfonamide 519174-22-2P,  
 (R)-N-[[2-[2-[2-Ethyl-4-(4-fluorobenzyl)piperazin-1-yl]-2-oxo-  
 ethoxy]-5-methylphenyl]acetyl]methanesulfonamide 519174-23-3P  
 , (R)-N-[3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-2-  
 oxoethoxy]phenyl]propionyl]methanesulfonamide 519174-24-4P,  
 N-[3-[2-[2-[4-(4-Fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-  
 oxoethoxy]-5-methylphenyl]propionyl]methanesulfonamide  
 519174-25-5P 519174-26-6P, (R)-N-[3-[5-Bromo-2-[2-[4-(4-  
 fluorobenzyl)-2-methylpiperazin-1-yl]-2-  
 oxoethoxy]phenyl]propionyl]methanesulfonamide 519174-27-7P  
 519174-28-8P, (R)-N-[3-[2-[2-[2-Ethyl-4-(4-fluorobenzyl)piperazin-  
 1-yl]-2-oxoethoxy]-5-methylphenyl]propionyl]methanesulfonamide  
 519174-29-9P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-  
 dimethylpiperazin-1-yl]-2-oxoethoxy]benzylamino]acetic acid  
 519174-30-2P, 3-[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-  
 dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acrylic acid  
 519174-31-3P, 3-[2-[2-[4-(4-Fluorobenzyl)-(2R,5S)-2,5-  
 dimethylpiperazin-1-yl]-2-oxoethoxy]-5-methylphenyl]acrylic acid  
 519174-32-4P, 3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-  
 methylpiperazin-1-yl]-2-oxoethoxy]phenyl]acrylic acid  
 519174-33-5P, 3-[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R)-2-  
 methylpiperazin-1-yl]-2-oxoethoxy]phenyl]acrylic acid  
 519174-34-6P, 5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-  
 dimethylpiperazin-1-yl]-2-oxoethoxy]-N-  
 [(ethylamino)carbonyl]benzenesulfonamide 519174-35-7P,  
 5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-  
 yl]-2-oxoethoxy]-N-[(phenylamino)carbonyl]benzenesulfonamide  
 519174-36-8P, 5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-  
 dimethylpiperazin-1-yl]-2-oxoethoxy]-N-[(2-  
 methylphenylamino)carbonyl]benzenesulfonamide 519174-37-9P,  
 5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-  
 yl]-2-oxoethoxy]-N-[(4-fluorophenylamino)carbonyl]benzenesulfonami  
 de 519174-38-0P, 5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-  
 dimethylpiperazin-1-yl]-2-oxoethoxy]-N-  
 (methoxycarbonyl)benzenesulfonamide 519174-39-1P,  
 5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-  
 yl]-2-oxoethoxy]-N-(ethoxycarbonyl)benzenesulfonamide  
 519174-40-4P, 5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-  
 dimethylpiperazin-1-yl]-2-oxoethoxy]-N-  
 isobutyrylbenzenesulfonamide 519174-41-5P, 5-Chloro-N-

(cyclopropylcarbonyl)-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzenesulfonamide  
519174-42-6P 519174-43-7P 519174-44-8P, [[[[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]sulfonyl]amino]-oxoacetic acid 519174-45-9P  
519174-47-1P, (R)-N-Acetyl-1-[5-chloro-2-[2-[4-(3,4-difluorobenzyl)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamide 519174-48-2P,  
(R)-N-Acetyl-1-[5-chloro-2-[2-[4-(4-chlorobenzyl)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamide  
519174-49-3P, (R)-[5-Chloro-2-[2-[4-(3,4-difluorobenzyl)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamide  
519174-50-6P, (R)-[5-Chloro-2-[2-[4-(4-chlorobenzyl)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamide  
519174-52-8P, 1-[5-Chloro-2-[2-[4-(3,4-difluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]-N-(cyclopropylcarbonyl)methanesulfonamide 519174-53-9P,  
1-[5-Chloro-2-[2-[4-(4-chlorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]-N-(trifluoroacetyl)methanesulfonamide  
519174-54-0P, [5-Chloro-2-[2-[(2R)-2-ethyl-4-(4-fluorobenzyl)piperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamide  
519174-55-1P, [5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamide  
519174-56-2P, [5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamide  
519174-57-3P, [5-Bromo-2-[2-[(2R)-2-ethyl-4-(4-fluorobenzyl)piperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamide  
519174-58-4P, N-Acetyl-1-[5-chloro-2-[2-[(2R)-2-ethyl-4-(4-fluorobenzyl)piperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamide  
519174-59-5P, N-Acetyl-1-[5-bromo-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamide  
519174-60-8P, N-Acetyl-1-[5-bromo-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamide  
519174-61-9P, N-Acetyl-1-[5-bromo-2-[2-[(2R)-2-ethyl-4-(4-fluorobenzyl)piperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamide  
519174-62-0P, 1-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]-N-(2,2-dimethylpropionyl)methanesulfonamide 519174-63-1P,  
[5-Chloro-2-[2-[4-(3,4-difluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamide  
519174-64-2P, [5-Chloro-2-[2-[4-(4-chlorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamide  
519174-65-3P, N-Acetyl-1-[5-chloro-2-[2-[4-(4-chlorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamide 519174-66-4P,  
1-[5-Chloro-2-[2-[4-(4-chlorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]-N-(cyclopropylcarbonyl)methanesulfonamide  
519174-67-5P 519174-68-6P 519174-69-7P,  
1-[5-Chloro-2-[2-[4-(3,4-difluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]-N-(cyclopropylcarbonyl)methanesulfonamide 519174-70-0P,  
[5-Bromo-2-[2-[4-(4-chlorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamide 519174-71-1P,  
N-Acetyl-1-[5-bromo-2-[2-[4-(4-chlorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamide  
519174-72-2P, N-Acetyl-1-[5-bromo-2-[2-[4-(4-chlorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamide  
519174-73-3P, [5-Bromo-2-[2-[4-(4-chlorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamide  
519174-74-4P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-

dimethylpiperazin-1-yl]-2-oxoethoxy]phenylmethanesulfonylamino]-oxoacetic acid 519174-75-5P, 1-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]-N-[(1-hydroxycyclopropyl)carbonyl]methanesulfonamide 519174-76-6P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenylmethanesulfonylamino]-oxoacetic acid 519174-77-7P, 1-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]-N-(methoxyacetyl)methanesulfonamide 519174-78-8P, N-Acetyl-1-[2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]-5-trifluoromethylphenyl]methanesulfonamide 519174-79-9P, N-Acetyl-1-[2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]-5-trifluoromethylphenyl]methanesulfonamide 519174-80-2P, [2-[2-[4-(4-Fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]-5-trifluoromethylphenyl]methanesulfonamide 519174-81-3P, [2-[2-[4-(4-Fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]-5-trifluoromethylphenyl]methanesulfonamide 519174-82-4P 519174-83-5P, 1-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]-N-(3-hydroxy-3-methylbutyryl)methanesulfonamide 519174-84-6P, 1-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]-N-(2-hydroxy-2-methylpropionyl)methanesulfonamide 519174-85-7P, 1-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]-N-(hydroxyacetyl)methanesulfonamide 519174-86-8P 519174-87-9P 519174-88-0P, 1-[5-Chloro-2-[2-[4-(4-chlorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]-N-(hydroxyacetyl)methanesulfonamide 519174-89-1P, 1-[5-Chloro-2-[2-[4-(3,4-difluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]-N-(hydroxyacetyl)methanesulfonamide 519174-90-4P, 1-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]-N-(3-hydroxy-3-methylbutyryl)methanesulfonamide 519174-91-5P, 1-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]-N-[(1-hydroxycyclopropyl)carbonyl]methanesulfonamide 519174-92-6P, 1-[2-[2-[4-(4-Fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]-5-trifluoromethylphenyl]-N-(hydroxyacetyl)methanesulfonamide 519174-93-7P, 1-[2-[2-[4-(4-Fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]-5-trifluoromethylphenyl]-N-(2-hydroxy-2-methylpropionyl)methanesulfonamide 519174-94-8P, 1-[2-[2-[4-(4-Fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]-5-trifluoromethylphenyl]-N-(2-hydroxy-2-methylpropionyl)methanesulfonamide 519174-95-9P, 1-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]-N-(methoxycarbonyl)methanesulfonamide 519174-96-0P, 1-[5-Chloro-2-[2-[4-(4-chlorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]-N-(methoxycarbonyl)methanesulfonamide 519174-97-1P, 1-[5-Chloro-2-[2-[4-(3,4-difluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]-N-(methoxycarbonyl)methanesulfonamide  
 (preparation of N-benzylpiperazine derivs. as chemokine receptor CCR1 antagonists useful as immunomodulatory agents)

L32 ANSWER 6 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2004:387265 HCAPLUS  
 DOCUMENT NUMBER: 140:391297



TITLE: Preparation of piperazine derivatives as CCR1 antagonists  
 INVENTOR(S): Blumberg, Laura Cook; Brown, Matthew Frank; Gaweco, Anderson See; Gladue, Ronald Paul; Hayward, Matthew Merrill; Lundquist, Gregory Dean; Poss, Christopher Stanley; Shavnya, Andre  
 PATENT ASSIGNEE(S): Pfizer Products Inc., USA  
 SOURCE: PCT Int. Appl., 131 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
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 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004039376	A1	20040513	WO 2003-IB4612	2003 1020

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

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CA 2498261	AA	20040513	CA 2003-2498261	2003 1020
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AU 2003269364	A1	20040525	AU 2003-269364	2003 1020
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BR 2003015777	A	20050913	BR 2003-15777	2003 1020
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EP 1583533	A1	20051012	EP 2003-751145	2003 1020
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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

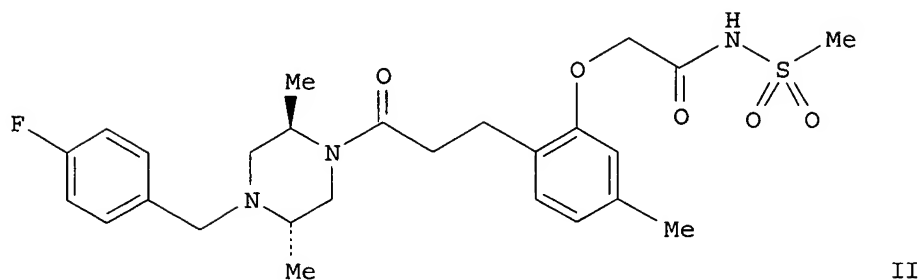
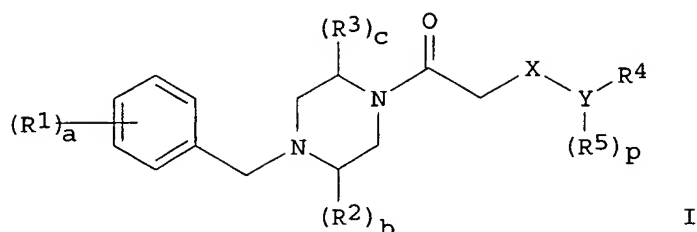
JP 2006506391	T2	20060223	JP 2004-547876	2003 1020
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PRIORITY APPLN. INFO.:	US 2002-422590P	P	2002 1030
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WO 2003-IB4612

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OTHER SOURCE(S) : MARPAT 140:391297  
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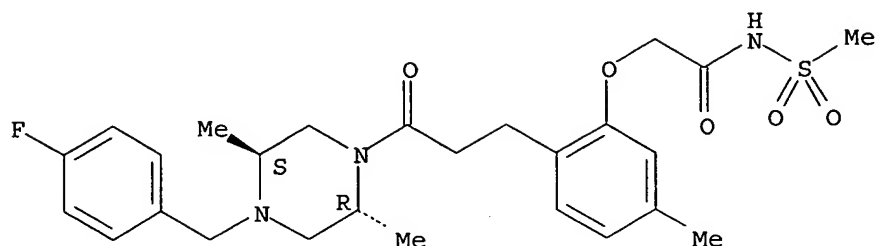
AB Title compds. I [a = 0-5; b,c = 0-2; p = 0-4; X = O, S, CH<sub>2</sub>, (un)substituted amino; Y = (hetero)aryl; R<sub>1</sub> = H, OH, halo, alkyl, alkoxy, etc.; R<sub>2</sub>-3 = H, oxo, (cyclo)alkyl, aryl, etc.; R<sub>4</sub> = alkyl, etc.; R<sub>5</sub> = H, OH, halo, CN, etc.] are prepared. For instance, (2R,5S)-1-(4-fluorobenzyl)-2,5-dimethylpiperazine (preparation given) is reacted with 7-methylchroman-2-one (PhMe, reflux 48 h), the resulting propanone treated with bromoacetic acid Me ester (THF, NaH) and the ester saponified to give II. All example compds. have IC<sub>50</sub> < 10 μM in the chemotaxis assay. I are useful for treating or preventing a disorder or condition that can be treated or prevented by antagonizing the CCR1 receptor in a mammal.

IT 519171-77-8P 519173-15-0P, N-[[2-[3-[4-(4-Fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-3-oxopropyl]-5-methoxyphenoxy]acetyl]methanesulfonamide  
(preparation of substituted N-acylpiperazine derivs. as CCR1 antagonists)

RN 519171-77-8 HCAPLUS

CN Acetamide, 2-[2-[3-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-3-oxopropyl]-5-methylphenoxy]-N-(methanesulfonyl)- (9CI) (CA INDEX NAME)

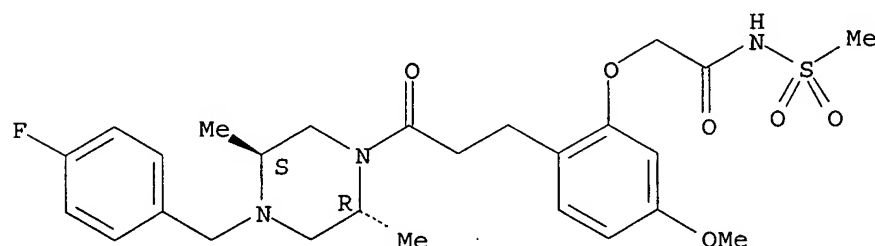
Absolute stereochemistry.



RN 519173-15-0 HCAPLUS

CN Acetamide, 2-[2-[3-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-3-oxopropyl]-5-methoxyphenoxy]-N-(methylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IC ICM A61K031-495

ICS A61P037-02

CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))  
Section cross-reference(s): 1, 63

IT Alzheimer's disease  
Anorexia  
Anti-Alzheimer's agents  
Anticholesteremic agents  
**Antidiabetic agents**  
Antiobesity agents  
Antitumor agents  
Bone resorption  
Cachexia  
Cardiovascular agents  
Cytomegalovirus  
**Diabetes insipidus**  
**Diabetes mellitus**  
Emphysema  
Encephalomyelitis  
Fibrosis  
Human  
Hyperplasia  
Inflammation  
Kidney, disease  
Lyme disease  
Malaria  
Mammary gland, neoplasm  
Meningitis  
Multiple myeloma

Neoplasm

Obesity

(preparation of substituted N-acylpiperazine derivs. as CCR1 antagonists)

IT 519171-77-8P 519171-85-8P, (2S)-2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]propionic acid 519171-92-7P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenylsulfamoyl]acetic acid 519171-93-8P, 3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzylamino]propionic acid hydrochloride 519171-96-1P 519171-98-3P, (2-Methylbenzenesulfonyl)carbamic acid 5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzyl ester 519171-99-4P, 2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzylsulfamoyl]propionic acid 519172-04-4P 519172-06-6P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzylideneaminoxy]acetic acid 519172-07-7P, N-[[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]methanesulfonamide 519172-09-9P, N-[[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]sulfamide 519172-10-2P, N-[3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]propionyl]methanesulfonamide 519172-14-6P, 3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acrylic acid 519172-16-8P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzenesulfonyl]amino]acetic acid hydrochloride 519172-21-5P, 5-Chloro-N-(2,2-dimethylpropionyl)-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzenesulfonamide 519172-22-6P, 5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]-N-(2-hydroxy-2-methylpropionyl)benzenesulfonamide 519172-30-6P 519172-32-8P 519172-33-9P, N-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]pyridin-3-yl]succinamic acid 519172-37-3P, N-[[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]pyridin-3-yl]acetyl]methanesulfonamide 519172-45-3P, 3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]pyridin-3-yl]propionic acid 519172-49-7P, [[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]amino]pyridine-3-carbonyl]amino]acetic acid 519172-55-5P, 2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenylsulfanyl]-2-methylpropionic acid 519172-59-9P, 2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzenesulfonyl]-2-methylpropionic acid 519172-62-4P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenylmethanesulfonyl]acetic acid 519172-65-7P, N-[3-[3-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]-6-methylpyridin-2-yl]propionyl]methanesulfonamide 519172-70-4P, 2-Amino-3-[5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]propionic acid 519172-73-7P, [[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzyl]methylamino]acetic acid 519172-75-9P, 2-[4-Chloro-2-(2H-tetrazol-5-ylmethoxy)phenoxy]-1-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]ethanone 519172-77-1P, 2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-

dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]nicotinic acid hydrochloride 519172-78-2P, [2-[2-[(2R)-2-Carbamoylmethyl-4-(4-fluorobenzyl)piperazin-1-yl]-2-oxoethoxy]-5-chlorophenoxy]acetic acid 519172-86-2P, (4S)-4-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]-1-methylpyrrolidine-(2S)-2-carboxylic acid dihydrochloride 519172-87-3P 519172-88-4P, 6-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]methyl]nicotinic acid 519172-90-8P, 5-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]-5-oxopentanoic acid 519172-94-2P, 5-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]dihydrofuran-2-one 519173-10-5P, 1-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]-2-(1H-tetrazol-5-yl)ethanone hydrochloride 519173-13-8P, 1-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]-3-(1H-tetrazol-5-yl)propan-1-one hydrochloride 519173-14-9P 519173-15-0P, N-[[2-[3-[4-(4-Fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-3-oxopropyl]-5-methoxyphenoxy]acetyl]methanesulfonamide 519173-16-1P, [5-Chloro-2-[3-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-3-oxopropyl]phenoxy]acetic acid 519173-17-2P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]oxoacetic acid 519173-18-3P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]acetic acid 519173-19-4P, N-[[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]acetyl]methanesulfonamide 519173-20-7P, [5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]acetic acid 519173-21-8P, [5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]acetic acid 519173-22-9P, [5-Chloro-2-[2-[(2R)-2-ethyl-4-(4-fluorobenzyl)piperazin-1-yl]-2-oxoethoxy]phenoxy]acetic acid 519173-23-0P, N-[[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]acetyl]methanesulfonamide 519173-24-1P, N-[[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]acetyl]methanesulfonamide 519173-25-2P, N-[[5-Chloro-2-[2-[(2R)-2-ethyl-4-(4-fluorobenzyl)piperazin-1-yl]-2-oxoethoxy]phenoxy]acetyl]methanesulfonamide 519173-26-3P, 2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]-2-methylpropionic acid 519173-27-4P, 4-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]butyric acid 519173-28-5P, 6-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]pyridine-2-carboxylic acid 519173-29-6P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]difluoroacetic acid 519173-30-9P, (2R)-2-Amino-4-[5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]butyric acid 519173-31-0P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]difluoroacetic acid 519173-32-1P, (R)-4-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]butanoic acid 519173-33-2P, 2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]-2-methylpropionic acid 519173-34-3P, (2S)-2-Amino-4-[5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]butyric acid 519173-35-4P, 2-[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-

2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]-2-methylpropionic acid 519173-36-5P, [5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]difluoroacetic acid 519173-37-6P, 2-[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]-2-methylpropionic acid 519173-38-7P, [5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]difluoroacetic acid 519173-39-8P, (2S)-2-Amino-4-[5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]butyric acid 519173-40-1P, (2S)-2-Amino-4-[5-bromo-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]butyric acid 519173-41-2P, 4-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]pyridine-2-carboxylic acid 519173-42-3P, N-[(2R)-2-Amino-4-[5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]butyryl]methanesulfonamide 519173-43-4P, 2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]methyl]thiazole-4-carboxylic acid 519173-44-5P, 3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]methyl]furan-2-carboxylic acid 519173-45-6P, 5-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]methyl]furan-2-carboxylic acid 519173-46-7P, 3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]methyl]thiophene-2-carboxylic acid 519173-47-8P, 2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]methyl]furan-3-carboxylic acid 519173-48-9P, 5-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]methyl]thiophene-2-carboxylic acid 519173-49-0P, 3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]methyl]furan-2-carboxylic acid 519173-50-3P, 3-[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]methyl]furan-2-carboxylic acid 519173-51-4P, 5-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]-5-(2-methoxyethyl)pyrimidine-2,4,6-trione 519173-53-6P, 5-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]-5-methylpyrimidine-2,4,6-trione 519173-55-8P, 5-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]-5-ethylpyrimidine-2,4,6-trione 519173-58-1P, (2R)-2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]propionic acid 519173-60-5P, (2S)-2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]propionic acid 519173-62-7P, (4S)-4-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]pyrrolidine-2-carboxylic acid 519173-63-8P, 3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]-2,2-dimethylpropionic acid 519173-65-0P, (4S)-4-[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenoxy]pyrrolidine-(2S)-2-carboxylic acid 519173-67-2P, (4S)-4-[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenoxy]pyrrolidine-(2S)-2-carboxylic acid 519173-70-7P, N-[(4S)-4-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-

oxoethoxy]phenoxy]pyrrolidine-(2S)-2-carbonyl]methanesulfonamide  
519173-72-9P 519173-73-0P 519173-74-1P 519173-75-2P  
519173-76-3P 519173-77-4P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-  
(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-  
oxoethoxy]benzylsulfamoyl]acetic acid 519173-78-5P  
519173-79-6P 519173-80-9P, [5-Bromo-2-[2-[4-(4-fluorobenzyl)-  
(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-  
oxoethoxy]benzylideneaminooxy]acetic acid 519173-81-0P,  
[1-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-  
dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]ethylideneaminooxy]acet  
ic acid 519173-82-1P, [1-[5-Bromo-2-[2-[4-(4-fluorobenzyl)-  
(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-  
oxoethoxy]phenyl]ethylideneaminooxy]acetic acid 519173-83-2P,  
[[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-  
1-yl]-2-oxoethoxy]phenyl]phenylmethyleneaminooxy]acetic acid  
519173-84-3P, [2-[2-[4-(4-Fluorobenzyl)-(2R,5S)-2,5-  
dimethylpiperazin-1-yl]-2-oxoethoxy]-5-  
methylbenzylideneaminooxy]acetic acid 519173-85-4P,  
(2S)-2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-  
dimethylpiperazin-1-yl]-2-oxoethoxy]benzyloxy]propionic acid  
519173-86-5P, (2R)-2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-  
2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzyloxy]propionic acid  
519173-87-6P, 2-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-  
dimethylpiperazin-1-yl]-2-oxoethoxy]benzyloxy]-2-methylpropionic  
acid 519173-88-7P, Methylsulfonylcarbamic acid  
5-chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-  
yl]-2-oxoethoxy]benzyl ester 519173-89-8P 519173-90-1P,  
N-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-  
2-oxoethoxy]benzoyl]methanesulfonamide 519173-91-2P  
519173-92-3P, N-[[5-Chloro-2-[2-[4-(4-fluorobenzyl)piperazin-1-yl]-  
2-oxoethoxy]phenyl]acetyl]methanesulfonamide 519173-93-4P  
519173-94-5P 519173-95-6P 519173-96-7P 519173-97-8P  
519173-98-9P 519173-99-0P 519174-00-6P, N-[[5-Bromo-2-[2-[4-(4-  
fluorobenzyl)piperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]methanesulf  
onamide 519174-01-7P, (R)-N-[[5-Chloro-2-[2-[4-(4-fluorobenzyl)-  
2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]methanesulfonami  
de 519174-02-8P, (R)-N-[[5-Bromo-2-[2-[4-(4-fluorobenzyl)-2-  
methylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]methanesulfonamide  
519174-03-9P 519174-04-0P 519174-05-1P 519174-06-2P  
519174-07-3P, Propane-2-sulfonic acid [[5-chloro-2-[2-[4-(4-  
fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-  
oxoethoxy]phenyl]acetyl]amide 519174-08-4P 519174-11-9P  
519174-12-0P, (R)-N-[[4-Chloro-2-[2-[4-(4-fluorobenzyl)-2-  
methylpiperazin-1-yl]-2-oxoethoxy]phenyl]acetyl]methanesulfonamide  
519174-13-1P 519174-14-2P 519174-15-3P 519174-16-4P  
519174-17-5P 519174-18-6P, (R)-N-[[5-Chloro-2-[2-[4-(4-  
chlorobenzyl)-2-methylpiperazin-1-yl]-2-  
oxoethoxy]phenyl]acetyl]methanesulfonamide 519174-19-7P,  
(R)-N-[[5-Chloro-2-[2-[4-(3,4-difluorobenzyl)-2-methylpiperazin-1-  
yl]-2-oxoethoxy]phenyl]acetyl]methanesulfonamide 519174-20-0P,  
(R)-N-[[5-Chloro-2-[2-[2-ethyl-4-(4-fluorobenzyl)piperazin-1-yl]-2-  
oxoethoxy]phenyl]acetyl]methanesulfonamide 519174-21-1P,  
(R)-N-[[5-Bromo-2-[2-[2-ethyl-4-(4-fluorobenzyl)piperazin-1-yl]-2-  
oxoethoxy]phenyl]acetyl]methanesulfonamide 519174-22-2P,  
(R)-N-[[2-[2-[2-Ethyl-4-(4-fluorobenzyl)piperazin-1-yl]-2-  
oxoethoxy]-5-methylphenyl]acetyl]methanesulfonamide  
519174-23-3P, (R)-N-[3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-2-  
methylpiperazin-1-yl]-2-oxoethoxy]phenyl]propionyl]methanesulfonam  
ide 519174-24-4P, N-[3-[2-[2-[4-(4-Fluorobenzyl)-(2R)-2-  
methylpiperazin-1-yl]-2-oxoethoxy]-5-methylphenyl]propionyl]methan

esulfonamide 519174-25-5P 519174-26-6P, (R)-N-[3-[5-Bromo-2-[2-[4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]propionyl]methanesulfonamide 519174-27-7P  
 519174-28-8P, (R)-N-[3-[2-[2-[2-Ethyl-4-(4-fluorobenzyl)piperazin-1-yl]-2-oxoethoxy]-5-methylphenyl]propionyl]methanesulfonamide  
 519174-29-9P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]benzylamino]acetic acid  
 519174-30-2P, 3-[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]acrylic acid  
 519174-31-3P, 3-[2-[2-[4-(4-Fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]-5-methylphenyl]acrylic acid  
 519174-32-4P, 3-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]acrylic acid  
 519174-33-5P, 3-[5-Bromo-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]acrylic acid  
 519174-34-6P 519174-35-7P 519174-36-8P 519174-37-9P  
 519174-38-0P 519174-39-1P 519174-40-4P 519174-41-5P  
 519174-42-6P 519174-43-7P 519174-44-8P 519174-45-9P  
 519174-52-8P, (R)-[5-Chloro-2-[2-[4-(3,4-difluorobenzyl)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]-N-((cyclopropane)carbonyl)methanesulfonamide 519174-53-9P,  
 (R)-[5-Chloro-2-[2-[4-(4-chlorobenzyl)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]-N-(trifluoroacetyl)methanesulfonamide  
 519174-62-0P 519174-63-1P, [5-Chloro-2-[2-[4-(3,4-difluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamide 519174-66-4P 519174-67-5P  
 519174-69-7P 519174-70-0P, [5-Bromo-2-[2-[4-(4-chlorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamide  
 519174-73-3P, [5-Bromo-2-[2-[4-(4-chlorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonamide  
 519174-74-4P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonylamino]oxoacetic acid 519174-75-5P 519174-76-6P, [5-Chloro-2-[2-[4-(4-fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]methanesulfonylamino]oxoacetic acid 519174-77-7P  
 519174-78-8P, (R)-N-Acetyl[2-[2-[4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-2-oxoethoxy]-5-trifluoromethylphenyl]methanesulfonamide 519174-79-9P 519174-80-2P, [2-[2-[4-(4-Fluorobenzyl)-(2R,5S)-2,5-dimethylpiperazin-1-yl]-2-oxoethoxy]-5-trifluoromethylphenyl]methanesulfonamide 519174-81-3P,  
 [2-[2-[4-(4-Fluorobenzyl)-(2R)-2-methylpiperazin-1-yl]-2-oxoethoxy]-5-trifluoromethylphenyl]methanesulfonamide  
 519174-82-4P 519174-83-5P 519174-84-6P, (R)-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]-N-(2-hydroxy-2-methylpropionyl)methanesulfonamide 519174-85-7P,  
 (R)-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]-N-(hydroxyacetyl)methanesulfonamide  
 519174-86-8P 519174-87-9P 519174-88-0P 519174-89-1P  
 519174-90-4P, (R)-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]-N-(3-hydroxy-3-methylbutyryl)methanesulfonamide 519174-91-5P,  
 (R)-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]-N-((1-hydroxycyclopropane)carbonyl)methanesulfonamide 519174-92-6P 519174-93-7P 519174-94-8P,  
 (R)-[2-[2-[4-(4-Fluorobenzyl)-2-methylpiperazin-1-yl]-2-oxoethoxy]-5-trifluoromethylphenyl]-N-(2-hydroxy-2-methylpropionyl)methanesulfonamide 519174-95-9P,  
 (R)-[5-Chloro-2-[2-[4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-2-oxoethoxy]phenyl]-N-(methoxycarbonyl)methanesulfonamide  
 519174-96-0P 519174-97-1P 519174-98-2P, N-[5-Chloro-2-[2-[4-(4-



fluorobenzyl) - (2R) -2-methylpiperazin-1-yl] -2-oxoethoxy]pyridin-3-yl] -2,2-dimethylsuccinamic acid 519174-99-3P,  
[[5-Chloro-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]pyridine-3-carbonyl]amino]acetic acid 519175-00-9P, N-[5-Chloro-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]pyridin-3-yl]succinamic acid 519175-01-0P, 3-[5-Chloro-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]pyridin-3-yl]acrylic acid 519175-02-1P, 3-[5-Chloro-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethylamino]pyridin-3-yl]propionic acid 519175-03-2P, N-[3-[5-Chloro-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]pyridin-3-yl]propionyl]methanesulfonamide 519175-04-3P, 2-Amino-3-[5-chloro-2-[2-[4-(4-fluorobenzyl) - (2R,5S) -2,5-dimethylpiperazin-1-yl] -2-oxoethoxy]pyridin-3-yl]propionic acid 519175-05-4P  
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 (preparation of substituted N-acylpiperazine derivs. as CCR1 antagonists)

L32 ANSWER 7 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:120834 HCAPLUS

DOCUMENT NUMBER: 140:181466

TITLE: Preparation of resorcinol derivatives as  
**peroxisome** proliferator-activated  
 receptor (PPAR)  $\gamma$ -agonists

INVENTOR(S): Shibata, Tomoyuki; Wada, Kunio; Nakamura,  
 Yuji; Araki, Kazushi

PATENT ASSIGNEE(S): Sankyo Company, Limited, Japan

SOURCE: PCT Int. Appl., 261 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

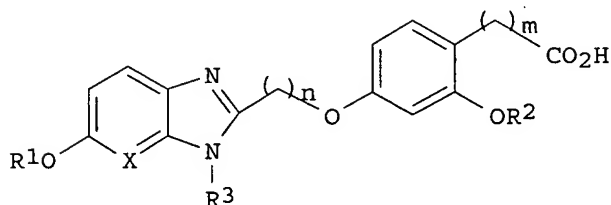
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2004013109	A1	20040212	WO 2003-JP9834	2003 0801

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OTHER SOURCE(S): MARPAT 140:181466  
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AB 4-[(Pyrido[2,3-d]imidazol-2-yl or benzimidazol-2-ylalkoxy)phenyl]propanoic acid or acetic acid derivs. represented by the following general formula (I) [wherein X = CH, N; R1 = each (un)substituted C1-6 alkyl, C3-10 cycloalkyl, C2-6 alkenyl, C6-10 aryl, C7-16 aralkyl, 4- to 10-membered heterocycle containing one to three heteroatoms selected from N, O, and S atoms; R2 = each (un)substituted C7-16 aralkyl, C9-16 aralkenyl, or alkyl substituted by a 5- to 10-membered heteroarom. ring containing one to three heteroatoms selected from N, O, and S atoms; R3 = H, C1-6 alkyl, (un)substituted C6-10 aryl; m = 1, 2; n = an integer of 1-3] or pharmacol. acceptable salts or esters thereof are prepared. Also disclosed are pharmaceutical compns. containing the compds. I or pharmacol. acceptable salts or esters thereof as the active ingredients (1) for improving insulin-resistance, lowering blood sugar, or inhibiting the proliferation of cancer cells or (2) for the prevention and/or treatment of **diabetes**, impaired glucose tolerance, obesity, hyperlipemia, or **diabetes** complications. Thus, 1.09 g 3-(2-benzyloxy-4-hydroxyphenyl)propionic acid Et ester and 697 mg 2-hydroxymethyl-6-methoxy-1-methyl-1H-benzimidazole were dissolved in 30 mL toluene, treated with 1.13 mL tributylphosphine and 1.14

g 1,1'-(azodicarbonyl)dipiperidine and stirred at room temperature overnight to give 87% 3-[2-benzyloxy-4-(6-methoxy-1-methyl-1H-benzimidazol-2-ylmethoxy)phenyl]propionic acid Et ester which (1.5 g) was stirred with a mixture of 7 mL EtOH, 7 mL THF, and 6.3 mL 1 N aqueous NaOH at room temperature overnight and stirred with 1 N aqueous HCl and EtOAc to give 45% 3-[2-benzyloxy-4-(6-methoxy-1-methyl-1H-benzimidazol-2-ylmethoxy)phenyl]propionic acid (II). 3-[4-[2-[6-(4-Amino-3,5-dimethylphenoxy)-1-methyl-1H-benzimidazol-2-yl]ethoxy]-2-(4-chlorobenzyloxy)phenyl]propionic acid hydrochloride was fed to male KK mice with a feed containing 0.01% II for 3 days to lower blood sugar level by 71%. A capsule, a tablet, and a granule containing I were formulated.

IT 657431-17-9P 657431-36-2P 657431-40-8P

657431-44-2P 657431-46-4P 657431-50-0P

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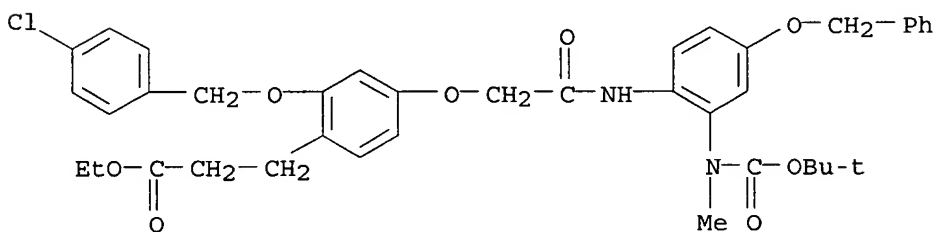
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(preparation of resorcinol derivs. as peroxisome proliferator-activated receptor (PPAR)  $\gamma$ -agonists, anticancer agents, or treatment or prevention of diabetes, impaired glucose tolerance, obesity, or hyperlipemia)

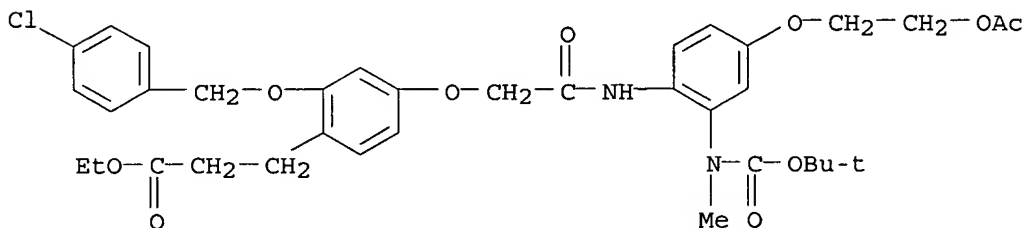
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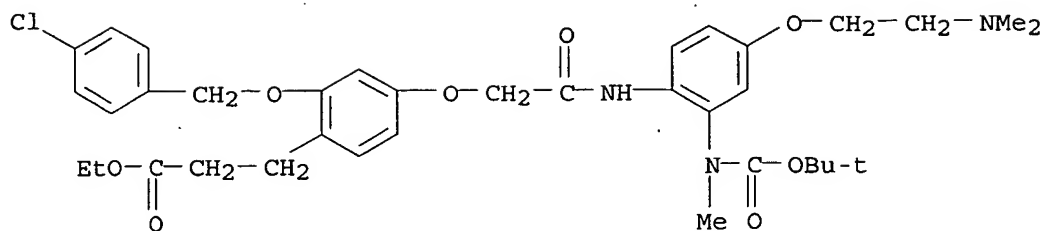
RN 657431-36-2 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[4-[2-(acetyloxy)ethoxy]-2-[[[(1,1-dimethylethoxy)carbonyl]methylamino]phenyl]amino]-2-oxoethoxy]-2-[[4-(chlorophenyl)methoxy]-, ethyl ester (9CI) (CA INDEX NAME)



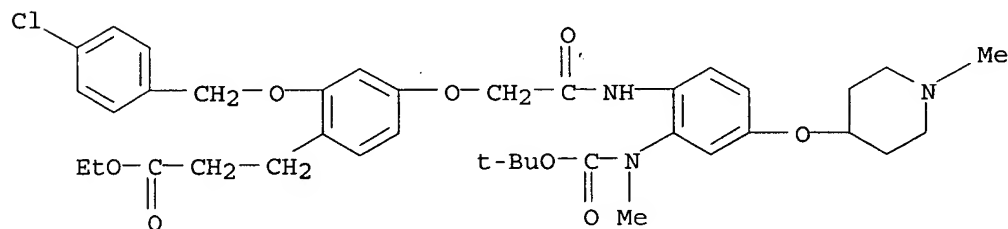
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RN 657431-44-2 HCAPLUS

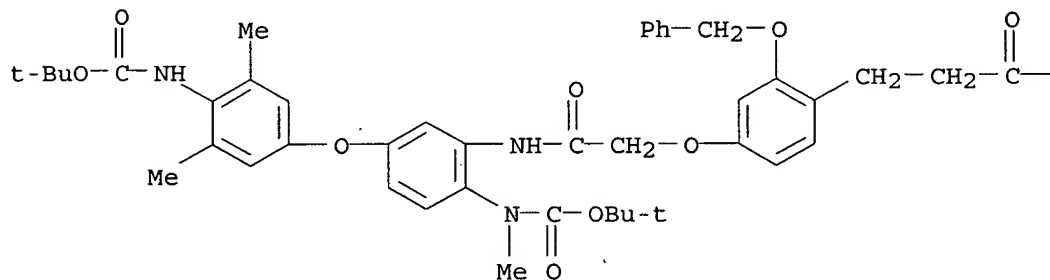
CN Benzenepropanoic acid, 2-[(4-chlorophenyl)methoxy]-4-[2-[[2-[(1,1-dimethylethoxy)carbonyl]methylamino]-4-[(1-methyl-4-piperidinyl)oxy]phenyl]amino]-2-oxoethoxy]-, ethyl ester (9CI)  
(CA INDEX NAME)



RN 657431-46-4 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[5-[4-[(1,1-dimethylethoxy)carbonyl]amino]-3,5-dimethylphenoxy]-2-[[[(1,1-dimethylethoxy)carbonyl]methylamino]phenyl]amino]-2-oxoethoxy]-2-(phenylmethoxy)-, ethyl ester (9CI) (CA INDEX NAME)

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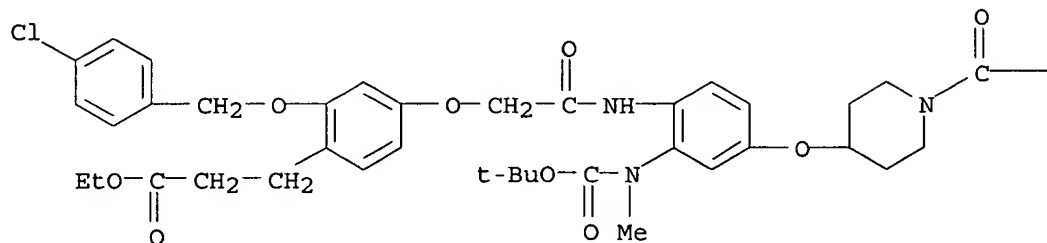
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RN 657431-50-0 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[4-[[[3-[(4-chlorophenyl)methoxy]-4-(3-ethoxy-3-oxopropyl)phenoxy]acetyl]amino]-3-[(1,1-

dimethylethoxy) carbonyl]methylamino]phenoxy]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

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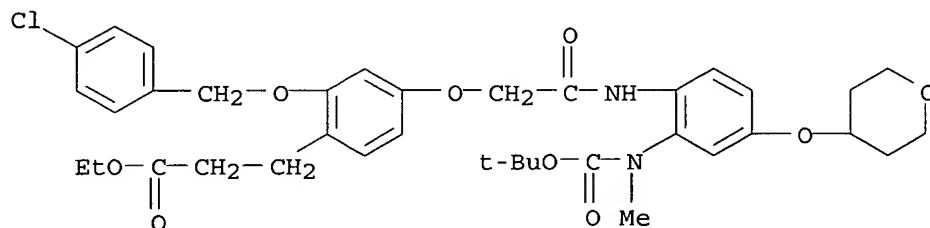


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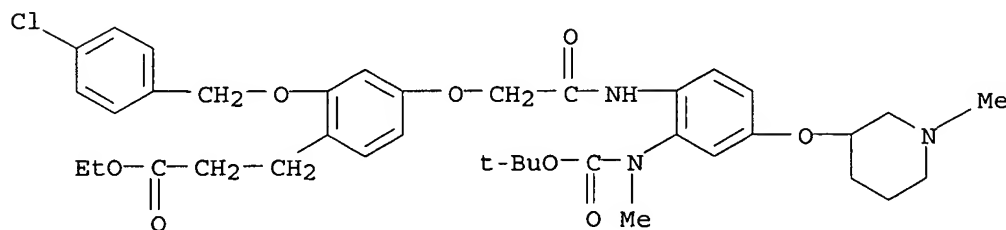
RN 657431-56-6 HCAPLUS

CN Benzenepropanoic acid, 2-[(4-chlorophenyl)methoxy]-4-[2-[[2-[(1,1-dimethylethoxy) carbonyl]methylamino]-4-[(tetrahydro-2H-pyran-4-yl)oxy]phenyl]amino]-2-oxoethoxy]-, ethyl ester (9CI) (CA INDEX NAME)



RN 657431-60-2 HCAPLUS

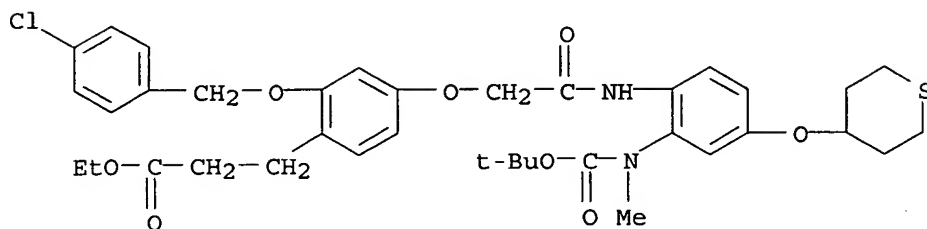
CN Benzenepropanoic acid, 2-[(4-chlorophenyl)methoxy]-4-[2-[[2-[(1,1-dimethylethoxy) carbonyl]methylamino]-4-[(1-methyl-3-piperidinyl)oxy]phenyl]amino]-2-oxoethoxy]-, ethyl ester (9CI) (CA INDEX NAME)



RN 657431-64-6 HCAPLUS

CN Benzenepropanoic acid, 2-[(4-chlorophenyl)methoxy]-4-[2-[[2-[(1,1-dimethylethoxy) carbonyl]methylamino]-4-[(tetrahydro-2H-thiopyran-4-

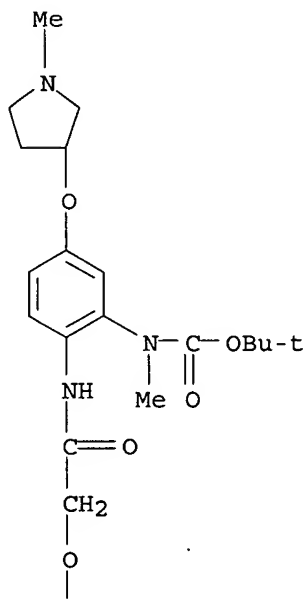
yl)oxy]phenyl]amino]-2-oxoethoxy]-, ethyl ester (9CI) (CA INDEX NAME)



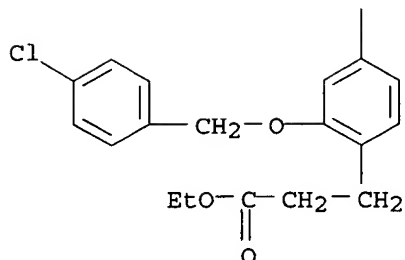
RN 657431-68-0 HCAPLUS

CN Benzenepropanoic acid, 2-[(4-chlorophenyl)methoxy]-4-[2-[[2-[[[(1,1-dimethylethoxy)carbonyl]methylamino]-4-[(1-methyl-3-pyrrolidinyl)oxy]phenyl]amino]-2-oxoethoxy]-, ethyl ester (9CI)  
(CA INDEX NAME)

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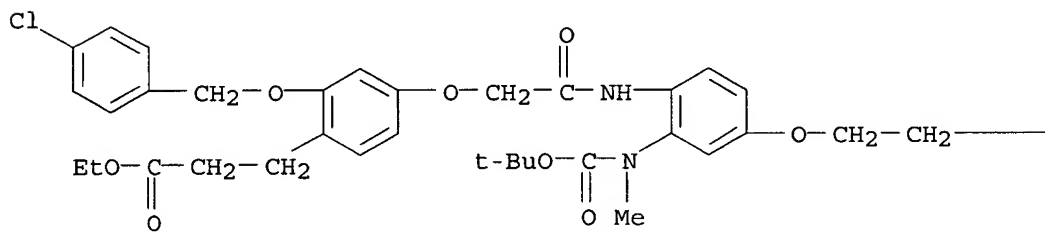


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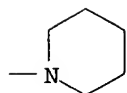


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 (CA INDEX NAME)

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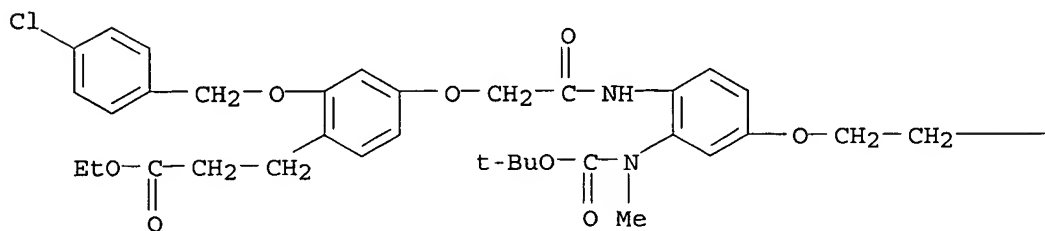


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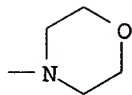
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 CN Benzenepropanoic acid, 2-[(4-chlorophenyl)methoxy]-4-[2-[[2-[(1,1-dimethylethoxy)carbonyl]methylamino]-4-[2-(4-morpholinyl)ethoxy]phenyl]amino]-2-oxoethoxy]-, ethyl ester (9CI)  
 (CA INDEX NAME)

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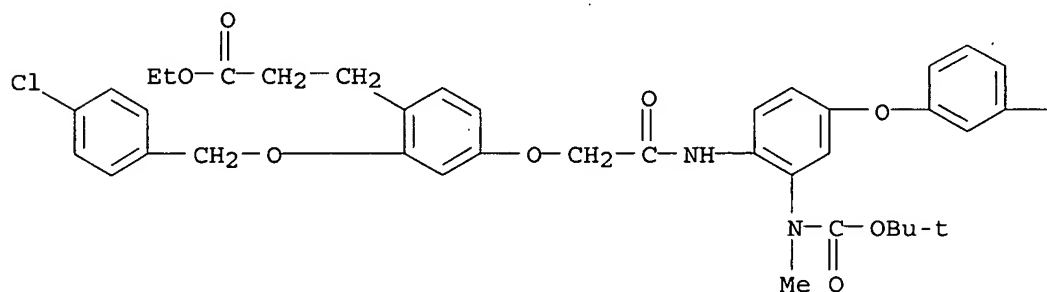


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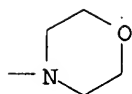


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 (CA INDEX NAME)

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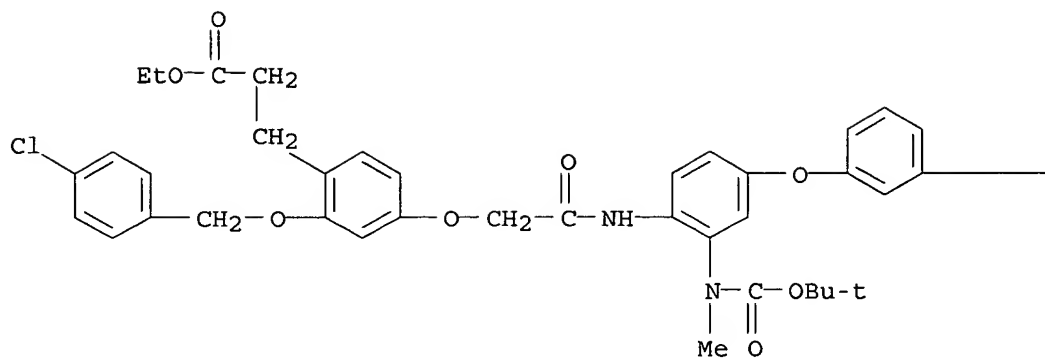


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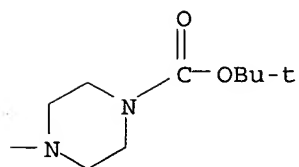


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 CN 1-Piperazinecarboxylic acid, 4-[3-[4-[[[3-[(4-chlorophenyl)methoxy]-4-(3-ethoxy-3-oxopropyl)phenoxy]acetyl]amino]-3-[(1,1-dimethylethoxy)carbonyl]methylamino]phenoxy]phenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

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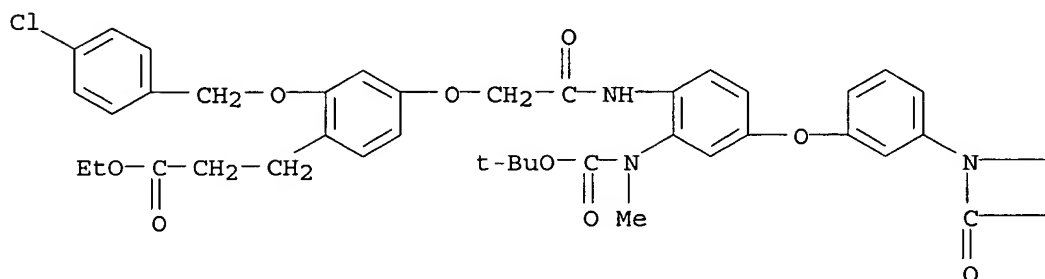
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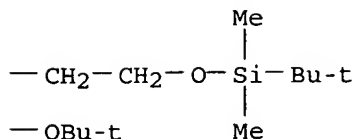
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PAGE 1-A



PAGE 1-B



- IC ICM C07D235-12  
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 A61P001-06
- CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))  
 Section cross-reference(s): 1
- ST resorcinol deriv prepn **peroxisome** proliferator activated  
 receptor gamma agonist; PPAR gamma agonist  
 benzimidazolylalkoxyphenylpropanoic acid prepn;  
 benzimidazolylmethoxyphenylpropionic acid prepn treatment  
**diabetes**; benzimidazolethoxyphenylpropionic acid prepn  
 treatment **diabetes**; impaired glucose tolerance treatment  
 prevention benzimidazolylalkoxyphenylpropanoic acid prepn; obesity  
 hyperlipemia treatment prevention benzimidazolylalkoxyphenylpropanoic  
 acid prepn; **diabetes** complication treatment  
 prevention benzimidazolylalkoxyphenylpropanoic acid prepn; insulin  
 resistance improver benzimidazolylalkoxyphenylpropanoic acid  
 prepn; blood sugar lowering benzimidazolylalkoxyphenylpropanoic  
 acid prepn; cancer proliferation inhibitor  
 benzimidazolylalkoxyphenylpropanoic acid prepn
- IT **Diabetes mellitus**  
 (diabetes complications; preparation of resorcinol derivs.  
 as **peroxisome** proliferator-activated receptor (PPAR)  
 γ-agonists, anticancer agents, or treatment or prevention  
 of **diabetes**, impaired glucose tolerance, obesity, or  
 hyperlipemia)
- IT **Antidiabetic agents**  
 Antiobesity agents  
 Antitumor agents  
**Diabetes mellitus**  
 Human  
 Hyperglycemia  
 Hypolipemic agents  
 Neoplasm  
 Obesity  
 (preparation of resorcinol derivs. as **peroxisome**  
 proliferator-activated receptor (PPAR) γ-agonists,  
 anticancer agents, or treatment or prevention of  
**diabetes**, impaired glucose tolerance, obesity, or  
 hyperlipemia)
- IT Hyperlipidemia  
 (preparation of resorcinol derivs. as **peroxisome**  
 proliferator-activated receptor (PPAR) γ-agonists,  
 anticancer agents, or treatment or prevention of  
**diabetes**, impaired glucose tolerance, obesity, or

hyperlipemia)

IT Peroxisome proliferator-activated receptors  
( $\gamma$ , agonists; preparation of resorcinol derivs. as  
peroxisome proliferator-activated receptor (PPAR)  
 $\gamma$ -agonists, anticancer agents, or treatment or prevention  
of **diabetes**, impaired glucose tolerance, obesity, or  
hyperlipemia)

IT 50-99-7, D-Glucose, biological studies  
(impaired glucose tolerance; preparation of resorcinol derivs. as  
peroxisome proliferator-activated receptor (PPAR)  
 $\gamma$ -agonists, anticancer agents, or treatment or prevention  
of **diabetes**, impaired glucose tolerance, obesity, or  
hyperlipemia)

IT 657429-24-8P 657429-25-9P 657429-26-0P 657429-27-1P  
657429-28-2P 657429-29-3P 657429-30-6P 657429-31-7P  
657429-32-8P 657429-33-9P 657429-34-0P 657429-35-1P  
657429-36-2P 657429-37-3P 657429-38-4P 657429-39-5P  
657429-40-8P 657429-41-9P 657429-42-0P 657429-43-1P  
657429-44-2P 657429-45-3P 657429-46-4P 657429-47-5P  
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657429-52-2P 657429-53-3P 657429-54-4P 657429-55-5P  
657429-56-6P 657429-57-7P 657429-58-8P 657429-59-9P  
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657429-64-6P 657429-65-7P 657429-66-8P 657429-67-9P  
657429-68-0P 657429-69-1P 657429-70-4P 657429-71-5P  
657429-72-6P 657429-73-7P 657429-74-8P 657429-75-9P  
657429-76-0P 657429-77-1P 657429-78-2P 657429-79-3P  
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657430-00-7P 657430-01-8P 657430-02-9P 657430-03-0P  
657430-04-1P 657430-05-2P 657430-06-3P 657430-07-4P  
657430-08-5P 657430-09-6P 657430-10-9P 657430-11-0P  
657430-12-1P 657430-13-2P 657430-14-3P 657430-15-4P  
657430-16-5P 657430-17-6P 657430-59-6P 657430-72-3P  
(preparation of resorcinol derivs. as **peroxisome**  
proliferator-activated receptor (PPAR)  $\gamma$ -agonists,  
anticancer agents, or treatment or prevention of  
**diabetes**, impaired glucose tolerance, obesity, or  
hyperlipemia)

IT 57-57-8, Oxetan-2-one 79-14-1, Glycolic acid, reactions  
94-99-5, 2,4-Dichlorobenzyl chloride 95-01-2,  
2,4-Dihydroxybenzaldehyde 96-41-3, Cyclopentanol 96-48-0,  
 $\gamma$ -Butyrolactone 100-39-0, Benzyl bromide 102-47-6,  
3,4-Dichlorobenzyl chloride 103-63-9, 2-Bromoethylbenzene  
104-81-4, 4-Methylbenzyl bromide 104-83-6, 4-Chlorobenzyl  
chloride 106-52-5, 1-Methylpiperidin-4-ol 107-18-6, Allyl  
alcohol, reactions 107-30-2, Chloromethyl methyl ether  
108-01-0, 2-Dimethylaminoethanol 108-93-0, Cyclohexanol,  
reactions 124-63-0, Methanesulfonyl chloride 395-44-8,  
2-Trifluoromethylbenzyl bromide 402-23-3, 3-  
Trifluoromethylbenzyl bromide 402-49-3, 4-Trifluoromethylbenzyl  
bromide 459-46-1, 4-Fluorobenzyl bromide 502-41-0,  
Cycloheptanol 542-59-6, 2-Acetoxyethanol 589-15-1,  
4-Bromobenzyl bromide 591-27-5, 3-Aminophenol 622-40-2,  
4-Morpholineethanol 637-59-2, 1-Bromo-3-phenylpropane  
824-94-2, 4-Methoxybenzyl chloride 867-13-0,  
Diethylphosphonoacetic acid ethyl ester 874-98-6,

3-Methoxybenzyl bromide 877-88-3, 3,5-Dimethoxybenzyl bromide 939-26-4, 2-Naphthylmethyl bromide 1592-20-7, 4-Vinylbenzyl chloride 1765-40-8, 1-Bromomethyl-2,3,4,5,6-pentafluorobenzene 1877-77-6, 3-Aminobenzyl alcohol 2014-83-7, 2,6-Dichlorobenzyl chloride 2051-18-5, 4-Isopropylbenzyl chloride 2081-44-9, 2567-29-5, 4-Phenylbenzyl bromide 2746-25-0, 4-Methoxybenzyl bromide 3040-44-6, 2-(Piperidin-1-yl)ethanol 3099-31-8, 3-Chloromethylpyridine 3447-53-8, 4-Difluoromethoxybenzyl bromide 3554-74-3, 1-Methylpiperidin-3-ol 4377-41-7, 2-Chloromethylquinoline 4392-24-9, Cinnamyl bromide 5292-43-3, tert-Butyl bromoacetate 5544-60-5, 4-Benzyloxybenzyl bromide 6653-80-1, 4-Ethoxybenzyl chloride 7311-46-8, 5-Bromo-2-chloromethylthiophene 13220-33-2, 1-Methylpyrrolidin-3-ol 16004-15-2, 4-Iodobenzyl bromide 18880-00-7, 4-tert-Butylbenzyl bromide 20034-71-3 23784-96-5, 2-Chloro-5-chloromethylthiophene 24424-99-5, Di-tert-butyl dicarbonate 27292-49-5, 3-(Morpholin-4-yl)phenol 29683-23-6, Tetrahydrothiopyran-4-ol 34776-73-3, 2-Chloromethyl-5-methylthiophene 38185-19-2, 4-Methylthiobenzyl bromide 50685-89-7 50824-05-0, 4-Trifluoromethoxybenzyl bromide 52289-93-7, 2-Methoxybenzyl bromide 53606-06-7 54751-01-8, 4-(Bromomethyl)pyridine 54777-65-0, 4-Acetylaminobenzyl chloride 57825-29-3, 2-Ethylbenzyl bromide 57825-30-6, 4-Ethylbenzyl bromide 59413-99-9 70258-18-3, 2-Chloro-5-chloromethylpyridine 86864-60-0, (2-Bromoethoxy)-tert-butyl dimethylsilane 109384-19-2, 4-Hydroxypiperidine-1-carboxylic acid tert-butyl ester 158985-25-2, 4-(4-Hydroxyphenyl)piperazine-1-carboxylic acid tert-butyl ester 170859-70-8, 4-Bromo-2-chloromethylthiophene 172648-24-7 185428-59-5 223134-15-4 299176-17-3 301548-21-0 301548-22-1 321595-75-9 337914-79-1 657431-19-1 657431-22-6 657431-29-3 657431-98-6

(preparation of resorcinol derivs. as peroxisome proliferator-activated receptor (PPAR)  $\gamma$ -agonists, anticancer agents, or treatment or prevention of diabetes, impaired glucose tolerance, obesity, or hyperlipemia)

IT 52085-14-0P, 4-Benzyloxy-2-hydroxybenzaldehyde 80754-22-9P  
 95332-26-6P, 2-Hydroxy-4-methoxymethoxybenzaldehyde 223133-34-4P  
 223133-36-6P 223133-38-8P 314271-24-4P 444646-76-8P  
 474295-91-5P 515164-47-3P 515164-48-4P 628334-62-3P  
 636563-05-8P 657430-18-7P 657430-19-8P 657430-20-1P  
 657430-21-2P 657430-22-3P 657430-23-4P 657430-24-5P  
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 657430-62-1P 657430-63-2P 657430-64-3P 657430-65-4P  
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657431-46-4P 657431-47-5P 657431-48-6P 657431-49-7P  
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657432-19-4P 657432-20-7P 657432-21-8P 657432-22-9P  
657432-23-0P 657432-24-1P 657432-25-2P 657432-26-3P  
657432-27-4P 657432-28-5P 657432-29-6P

(preparation of resorcinol derivs. as **peroxisome**  
proliferator-activated receptor (PPAR)  $\gamma$ -agonists,  
anticancer agents, or treatment or prevention of  
**diabetes**, impaired glucose tolerance, obesity, or  
hyperlipemia)

IT 9004-10-8, Insulin, biological studies  
(resistance; preparation of resorcinol derivs. as **peroxisome**  
proliferator-activated receptor (PPAR)  $\gamma$ -agonists,  
anticancer agents, or treatment or prevention of  
**diabetes**, impaired glucose tolerance, obesity, or  
hyperlipemia)

L32 ANSWER 8 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:80638 HCAPLUS

DOCUMENT NUMBER: 140:128152

TITLE: Preparation of benzoic acids, in particular  
acetylaminobenzoic acids, as promoters of  
nonsense mutation suppression in messenger RNA  
(mRNA) and/or as modulators of translation

INVENTOR(S): Wilde, Richard G.; Welch., Ellen M.; Takasugi,  
James Jan; Almstead, Neil G.; Rubenstein,  
Steven Marc; Beckmann, Holger

PATENT ASSIGNEE(S): PTC Therapeutics, Inc., USA; Tularik Inc.

SOURCE: PCT Int. Appl., 112 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004009533	A1	20040129	WO 2003-US23183	2003 0723

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W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2493457	AA	20040129	CA 2003-2493457	2003 0723
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AU 2003254157	A1	20040209	AU 2003-254157	2003 0723
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EP 1525185	A1	20050427	EP 2003-766013	2003 0723
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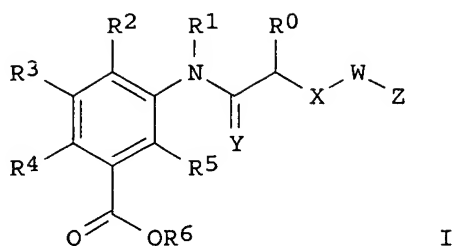
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PRIORITY APPLN. INFO.:	US 2002-398267P	P	2002 0724
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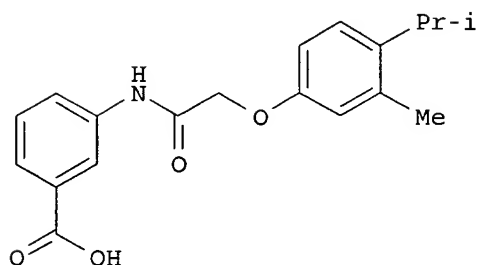
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WO 2003-US23183	W	2003 0723
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OTHER SOURCE(S): MARPAT 140:128152  
 GI



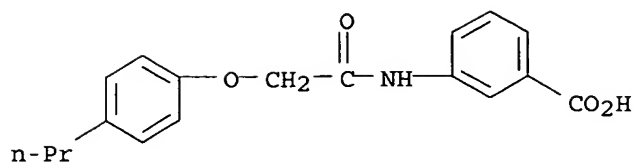
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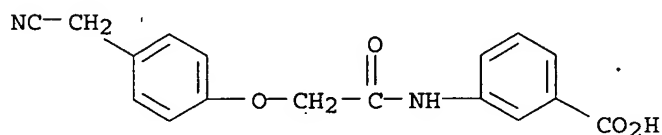
II

- AB Title compds. I [wherein X = O, S, CO, SO, SO<sub>2</sub>; Y = O, S; Z = (un)substituted hetero/aryl, cycloalkyl; W = (CH<sub>2</sub>)<sub>n</sub>; n = 0-4; R<sub>1</sub> = H, SO<sub>2</sub>H and derivs., CF<sub>3</sub>, CN, CO<sub>2</sub>H and derivs., CHO and derivs., (un)substituted alk(en/yn)yl, hetero/cycloalkyl, hetero/aryl; R<sub>0</sub> = H or R<sub>0</sub>CCNR<sub>1</sub> = 5-7 membered heterocyclyl or heteroaryl ring; R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub>, R<sub>5</sub> = independently H, halo, CF<sub>3</sub>, OCF<sub>3</sub>, OCHF<sub>2</sub>, CN, CO<sub>2</sub>H and derivs., SO<sub>2</sub>H and derivs., NO<sub>2</sub>, NH<sub>2</sub> and derivs., (un)substituted alk(en/yn)yl, (un)substituted hetero/cycloalkyl, hetero/aryl, alkoxy, hetero/aryloxy; R<sub>6</sub> = H, (un)substituted cyclo/heterocyclo/alkyl, hetero/aryl, or any biohydrolyzable group; their pharmaceutical acceptable salts, hydrates, clathrates, prodrugs, polymorphs, and stereoisomers] were prepared as promoters of nonsense mutation suppression in mRNA (mRNA) and/or as modulators of translation termination. For example, II was prepared in 3 steps by acylation of Me 3-aminobenzoate with bromoacetyl bromide in the presence of DIPEA/THF, O-arylation of 4-isopropyl-3-methylphenol with the bromide intermediate in the presence of K<sub>2</sub>CO<sub>3</sub>/2-butanone, and demethylation. II showed both very high potency and efficacy of protein synthesis in a cell-based luciferase assay (no data). Thus, I are useful for treating or preventing a disease ameliorated by modulation of premature translation termination or nonsense-mediated mRNA decay, or ameliorating one or more symptoms associated therewith.
- IT 649773-67-1P, 3-[[2-(4-Propylphenoxy)acetyl]amino]benzoic acid 649774-21-0P, 3-[[2-[(4-Cyanomethylphenyl)oxy]acetyl]amino]benzoic acid (promotor of nonsense mutation suppression; preparation of benzoic acids, in particular acetylaminobenzoic acids, as promoters of nonsense mutation suppression in mRNA and/or as modulators of translation termination)
- RN 649773-67-1 HCAPLUS
- CN Benzoic acid, 3-[[[(4-propylphenoxy)acetyl]amino]- (9CI) (CA INDEX NAME)





RN 649774-21-0 HCAPLUS  
 CN Benzoic acid, 3-[[[4-(cyanomethyl)phenoxy]acetyl]amino] - (9CI)  
 (CA INDEX NAME)



IC ICM C07C235-24  
 ICS C07C323-63; C07C327-42; C07D207-273; C07D405-12; C07D317-64;  
 C07D213-64; C07D209-48; C07D239-38; C07D257-04; C07D271-06;  
 A61K031-16; A61K031-33; A61P003-00; A61P007-00  
 CC 25-17 (Benzene, Its Derivatives, and Condensed Benzenoid  
 Compounds)  
 Section cross-reference(s): 1, 63  
 IT Anti-Alzheimer's agents  
 Anti-inflammatory agents  
 Antiarthritics  
 Anticholesteremic agents  
 Antidiabetic agents  
 Antiobesity agents  
 Antiparkinsonian agents  
 Antirheumatic agents  
 Antitumor agents  
 Human  
 Nervous system agents  
 (preparation of benzoic acids, in particular acetylamino benzoic  
 acids, as promoters of nonsense mutation suppression in mRNA  
 and/or as modulators of translation termination)  
 IT Acute B-cell leukemia  
 Acute T-cell leukemia  
 Acute lymphocytic leukemia  
 Acute myeloid leukemia  
 Acute myeloid leukemia  
 Acute myelomonocytic leukemia  
 Acute promyelocytic leukemia  
 Adrenal gland, neoplasm  
 Aging, animal  
 Alzheimer's disease  
 Amyloidosis  
 Arthritis  
 Atherosclerosis  
 Blood, disease  
 Bone, neoplasm  
 Brain, neoplasm  
 Carcinoma

Central nervous system, disease

Chronic lymphocytic leukemia

Chronic myeloid leukemia

Cirrhosis

Cystic fibrosis

**Diabetes** mellitus

Dwarfism

Esophagus, neoplasm

Eye, neoplasm

Familial hypercholesterolemia

Hairy cell leukemia

Head and Neck, neoplasm

Head and Neck, neoplasm

Heart, disease

Hematopoietic neoplasm

Hyperthyroidism

Hypothyroidism

Immunodeficiency

Inflammation

Intestine, neoplasm

Kidney, disease

Kidney, neoplasm

Liver, neoplasm

Lung, neoplasm

Mammary gland, neoplasm

Marfan syndrome

Melanoma

Mouth, neoplasm

Multiple myeloma

Multiple sclerosis

Muscular dystrophy

Neoplasm

Neuroglia, neoplasm

Niemann-Pick disease

Obesity

Ovary, neoplasm

Pancreas, neoplasm

Parkinson's disease

Pharynx, neoplasm

Prostate gland, neoplasm

Rheumatoid arthritis

Sarcoma

Skin, neoplasm

Stomach, neoplasm

Testis, neoplasm

(treatment; preparation of benzoic acids, in particular  
acetylaminobenzoic acids, as promoters of nonsense mutation  
suppression in mRNA and/or as modulators of translation  
termination)

- IT 70853-28-0P, 3-[[2-(4-Chlorophenoxy)acetyl]amino]benzoic acid  
82157-40-2P, 3-[[2-(p-Tolyloxy)acetyl]amino]benzoic acid  
303773-82-2P, 3-[[2-[(Naphthalen-2-yl)oxy]acetyl]amino]benzoic  
acid 304890-52-6P, 3-[[2-(2-Isopropylphenyloxy)acetyl]amino]benz  
oic acid 319489-60-6P, 3-[[2-(3,4-Dimethylphenoxy)acetyl]amino]b  
enzoic acid 397281-31-1P, 3-[[2-(4-Bromophenoxy)acetyl]amino]ben  
zoic acid 397281-40-2P, 3-[[2-(4-Phenoxyphenoxy)acetyl]amino]ben  
zoic acid 397282-38-1P, 3-[[2-(4-Acetylphenyloxy)acetyl]amino]be  
nzoic acid 405921-06-4P, 3-[[2-(4-tert-  
Butylphenoxy)acetyl]amino]benzoic acid 405924-15-4P,  
3-[[2-[4-(1-Methyl-1-phenylethyl)phenoxy]acetyl]amino]benzoic acid

405924-18-7P, 3-[[2-[(4'-Methyl-1,1'-biphen-4-yl)oxy]acetyl]amino]benzoic acid 446829-09-0P,  
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649773-62-6P, 3-[[2-(4-Isopropyl-3-methylphenoxy)-1-  
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3-[[2-[(2'-Methyl-1,1'-biphen-4-yl)oxy]acetyl]amino]benzoic acid  
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yl)oxy]acetyl]amino]benzoic acid 649773-65-9P,  
3-[[2-(3,4-Dichlorophenoxy)acetyl]amino]benzoic acid  
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649773-69-3P, 3-[[2-(4-Ethylphenyloxy)acetyl]amino]benzoic acid  
649773-70-6P, 3-[[2-[(Indan-5-yl)oxy]acetyl]amino]benzoic acid  
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no]benzoic acid 649773-96-6P, 3-[[2-[(4-Isopropyl-3-  
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REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

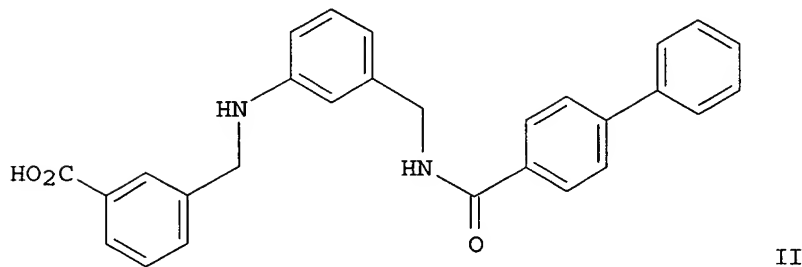
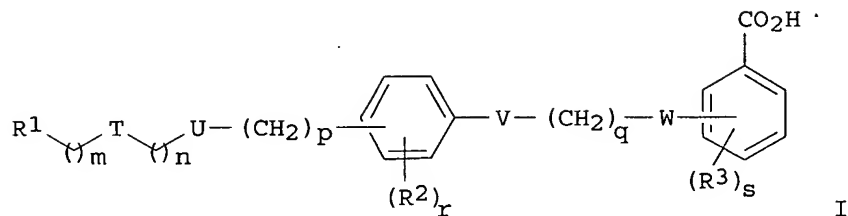
L32 ANSWER 9 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2004:2679 HCAPLUS  
 DOCUMENT NUMBER: 140:76898

TITLE: Preparation of benzoic acid derivatives as  
 modulators of PPAR- $\alpha$  and PPAR- $\gamma$   
 INVENTOR(S): Li, Lanna  
 PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited  
 SOURCE: PCT Int. Appl., 101 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004000295	A1	20031231	WO 2003-GB2598	2003 0617
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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AU 2003240101	A1	20040106	AU 2003-240101	2003 0617
BR 2003011840	A	20050315	BR 2003-11840	2003 0617
EP 1517680	A1	20050330	EP 2003-732715	2003 0617
CN 1662230	A	20050831	CN 2003-814319	2003 0617
JP 2006502105	T2	20060119	JP 2004-515010	2003 0617
NZ 536972	A	20060630	NZ 2003-536972	2003 0617

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US 2005267149	A1	20051201	US 2004-518819	2004 1220
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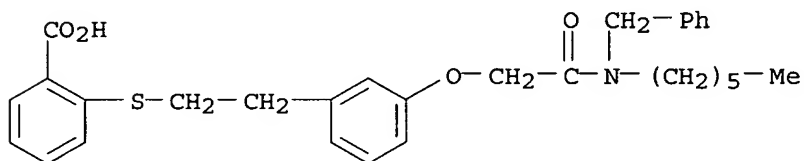
OTHER SOURCE(S): MARPAT 140:76898  
GI



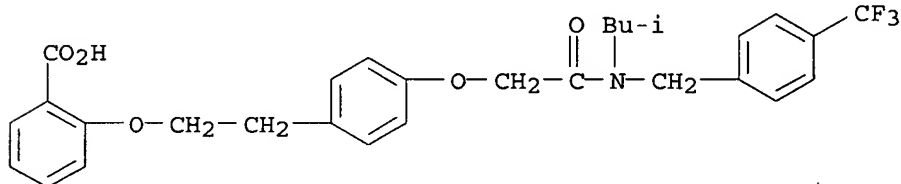
AB Title compds. I [R1 = (un)substituted aryl, alkyl, acyl, etc.; (CH2)m-T-(CH2)n-U-(CH2)p = attached at either the meta or para position (to V) and is O(CH2)2, O(CH2)3, etc.; V = O, S, amino, single bond; q = 1-3; W = O, S, amido, amino, single bond; R2 = halo, alkyl, alkoxy, etc.; r = 0-3; R3 = halo, alkyl, alkoxy, etc.; s = 0-3; with some provisions] are prepared For instance, tert-Bu [3-[[[(1,1'-biphenyl-4-yl)carbonyl]amino]methyl]phenyl]car

bamate (preparation given) is deprotected (CH<sub>2</sub>Cl<sub>2</sub>, TFA) and alkylated with 3-carboxybenzaldehyde (HOAc, NaBH<sub>4</sub>) to give II. Compds. of the invention have an EC<sub>50</sub> < 50 μmol/L for PPAR-α and PPAR-γ. I are useful in treating clin. conditions associated with insulin resistance.

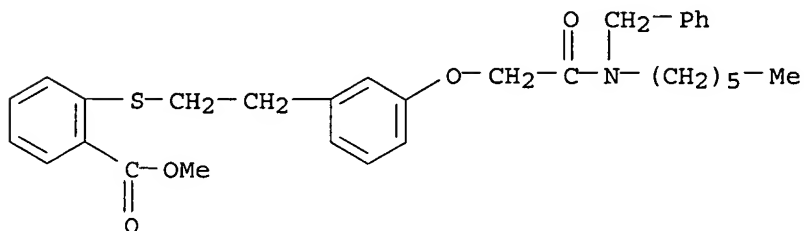
- IT 637358-95-3P, 2-[[2-[3-[2-[Benzyl(hexyl)amino]-2-oxoethoxy]phenyl]ethyl]thio]benzoic acid 637359-18-3P, 2-[2-[4-[2-[Isobutyl[4-(trifluoromethyl)benzyl]amino]-2-oxoethoxy]phenyl]ethoxy]benzoic acid (preparation of benzoic acid derivs. as modulators of PPAR-α and PPAR-γ)
- RN 637358-95-3 HCAPLUS
- CN Benzoic acid, 2-[[2-[3-[2-[hexyl(phenylmethyl)amino]-2-oxoethoxy]phenyl]ethyl]thio]- (9CI) (CA INDEX NAME)



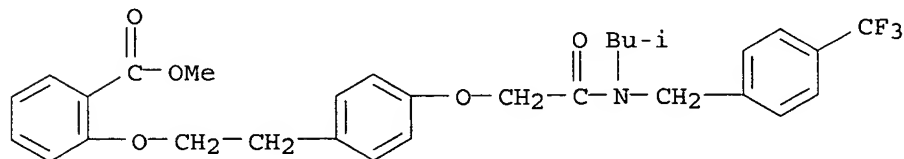
- RN 637359-18-3 HCAPLUS
- CN Benzoic acid, 2-[2-[4-[2-[(2-methylpropyl)[[4-(trifluoromethyl)phenyl]methyl]amino]-2-oxoethoxy]phenyl]ethoxy]- (9CI) (CA INDEX NAME)



- IT 637358-94-2P, Methyl 2-[[2-[3-[2-[benzyl(hexyl)amino]-2-oxoethoxy]phenyl]ethyl]thio]benzoate 637359-17-2P,, Methyl 2-[2-[4-[2-[isobutyl[4-(trifluoromethyl)benzyl]amino]-2-oxoethoxy]phenyl]ethoxy]benzoate (preparation of benzoic acid derivs. as modulators of PPAR-α and PPAR-γ)
- RN 637358-94-2 HCAPLUS
- CN Benzoic acid, 2-[[2-[3-[2-[hexyl(phenylmethyl)amino]-2-oxoethoxy]phenyl]ethyl]thio]-, methyl ester (9CI) (CA INDEX NAME)



RN 637359-17-2 HCAPLUS  
 CN Benzoic acid, 2-[2-[4-[2-[(2-methylpropyl)[[4-(trifluoromethyl)phenyl]methyl]amino]-2-oxoethoxy]phenyl]ethoxy]-, methyl ester (9CI) (CA INDEX NAME)



IC ICM A61K031-19  
 ICS A61P003-06; A61P003-10; C07C065-24; C07C233-78; C07C235-34;  
 C07C309-66; C07C311-13; C07C323-62; C07D213-40; C07D217-06;  
 C07D277-56; C07D307-68; C07D233-60  
 CC 25-17 (Benzene, Its Derivatives, and Condensed Benzenoid  
 Compounds)  
 Section cross-reference(s): 1, 63  
 IT **Peroxisome** proliferator-activated receptors  
 (α; preparation of benzoic acid derivs. as modulators of  
 PPAR-α and PPAR-γ)  
 IT **Peroxisome** proliferator-activated receptors  
 (γ; preparation of benzoic acid derivs. as modulators of  
 PPAR-α and PPAR-γ)  
 IT 637358-29-3P, 3-[[[3-[[[(1,1'-Biphenyl-4-yl)carbonyl]amino]methyl]phenyl]amino]methyl]benzoic acid  
 637358-31-7P, 2-[[4-[2-Oxo-2-[[4-(trifluoromethyl)benzyl]amino]ethyl]phenoxy]methyl]benzoic acid 637358-36-2P,  
 2-[[3-[2-[Benzyl(hexyl)amino]-2-oxoethyl]phenoxy]methyl]benzoic acid 637358-40-8P, 2-[[3-[2-Oxo-2-[[4-(trifluoromethyl)benzyl]amino]ethyl]phenoxy]methyl]benzoic acid  
 637358-44-2P, 2-[[4-[3-[[2-(3,4-Dimethoxyphenyl)ethyl](methyl)amino]-3-oxopropyl]phenoxy]methyl]benzoic acid 637358-47-5P,  
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 637358-56-6P, 2-[[4-[2-[Benzyl(hexyl)amino]-2-oxoethyl]-2-fluorophenoxy]methyl]benzoic acid 637358-59-9P,  
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 2-[[4-[3-(1,2,3,4-Tetrahydroisoquinolin-2-yl)-3-oxopropyl]phenoxy]methyl]benzoic acid 637358-66-8P,  
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 2-[[4-[3-[4-(Benzyloxy)phenoxy]propyl]phenoxy]methyl]benzoic acid 637358-82-8P, 2-[[4-[3-[4-[(Methylsulfonyl)oxy]phenoxy]propyl]phenoxy]methyl]benzoic acid 637358-83-9P, 2-[[4-[3-(4-Hydroxyphenoxy)propyl]phenoxy]methyl]benzoic acid 637358-86-2P,



2-[[4-[3-[[2-(2-Ethoxyphenyl)ethyl]amino]-3-oxopropyl]phenoxy]methyl]benzoic acid 637358-89-5P,  
 2-[[4-[3-[Ethyl(2-(pyridin-2-yl)ethyl)amino]-3-oxopropyl]phenoxy]methyl]benzoic acid 637358-95-3P,  
 2-[[2-[3-[2-[Benzyl(hexyl)amino]-2-oxoethoxy]phenyl]ethyl]thio]benzoic acid 637358-98-6P, 2-[[4-[2-[Heptyl[2-(2-methoxyphenyl)ethyl]amino]-2-oxoethyl]phenoxy]methyl]benzoic acid 637359-01-4P, 2-[[4-[2-[[2-(4-Chlorophenyl)ethyl](heptyl)amino]-2-oxoethyl]phenoxy]methyl]benzoic acid 637359-04-7P,  
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 2-[[4-[2-[Ethyl(2-fluorobenzyl)amino]-2-oxoethoxy]phenoxy]methyl]benzoic acid 637359-10-5P,  
 2-[[4-[2-[Ethyl(2-fluorobenzyl)amino]-2-oxoethyl]benzyl]oxy]benzoic acid 637359-12-7P,  
 2-[[4-[2-[Heptyl(2-phenylethyl)amino]-2-oxoethyl]benzyl]oxy]benzoic acid 637359-14-9P,  
 2-[[4-[2-[[2-(4-Chlorophenyl)ethyl](heptyl)amino]-2-oxoethyl]benzyl]oxy]benzoic acid 637359-18-3P,  
 2-[2-[4-[2-[Isobutyl[4-(trifluoromethyl)benzyl]amino]-2-oxoethoxy]phenyl]ethoxy]benzoic acid

(preparation of benzoic acid derivs. as modulators of PPAR- $\alpha$  and PPAR- $\gamma$ )

IT 135810-05-8P, Methyl 2-[[4-(3-hydroxypropyl)phenoxy]methyl]benzoate 211917-72-5P, Methyl 2-[[4-[2-[(tert-butoxycarbonyl)amino]ethyl]phenoxy]methyl]benzoate 265996-88-1P, N-Heptyl-2-phenylacetamide 348613-09-2P, N-Heptyl-2-(2-methoxyphenyl)acetamide 349428-15-5P, 2-(4-Chlorophenyl)-N-heptylacetamide 637358-27-1P, tert-Butyl [3-[[[(1,1'-biphenyl-4-yl)carbonyl]amino]methyl]phenyl]carbamate 637358-28-2P, N-(3-Aminobenzyl)-1,1'-biphenyl-4-carboxamide 637358-30-6P, Methyl 2-[[4-[2-oxo-2-[[4-(trifluoromethyl)benzyl]amino]ethyl]phenoxy]methyl]benzoate 637358-32-8P, [3-[[2-(Methoxycarbonyl)benzyl]oxy]phenyl]acetic acid 637358-34-0P, Methyl 2-[[3-[2-[benzyl(hexyl)amino]-2-oxoethyl]phenoxy]methyl]benzoate 637358-38-4P, Methyl 2-[[3-[2-oxo-2-[[4-(trifluoromethyl)benzyl]amino]ethyl]phenoxy]methyl]benzoate 637358-42-0P, N-[2-(3,4-Dimethoxyphenyl)ethyl]-3-(4-hydroxyphenyl)-N-(methyl)propanamide 637358-43-1P, Methyl 2-[[4-[3-[2-(3,4-dimethoxyphenyl)ethyl(methyl)amino]-3-oxopropyl]phenoxy]methyl]benzoate 637358-45-3P, Methyl 2-[[4-(2-aminoethyl)phenoxy]methyl]benzoate hydrochloride 637358-46-4P, Methyl 2-[[4-[2-[[4-methyl-2-(4-(trifluoromethyl)phenyl)thiazol-5-yl]carbonyl]amino]ethyl]phenoxy]methyl]benzoate 637358-48-6P, Methyl 2-[[4-[2-[[[(2,4-difluorophenyl)amino]carbonyl]amino]ethyl]phenoxy]methyl]benzoate 637358-50-0P, Methyl 2-[[4-[2-[[2-methyl-5-phenylfuran-3-yl]carbonyl]amino]ethyl]phenoxy]methyl]benzoate 637358-52-2P, Methyl 2-[[4-[2-[(benzylsulfonyl)amino]ethyl]phenoxy]methyl]benzoate 637358-54-4P, N-Benzyl-2-(3-fluoro-4-hydroxyphenyl)-N-hexylacetamide 637358-55-5P, Methyl 2-[[4-[2-[benzyl(hexyl)amino]-2-oxoethyl]-2-fluorophenoxy]methyl]benzoate 637358-57-7P, N-Benzyl-N-hexyl-2-(4-hydroxy-3-methoxyphenyl)acetamide 637358-58-8P, Methyl 2-[[4-[2-[benzyl(hexyl)amino]-2-oxoethyl]-2-(methoxy)phenoxy]methyl]benzoate 637358-60-2P 637358-61-3P 637358-63-5P, Methyl 2-[[4-(2-hydroxyethyl)phenoxy]methyl]benzoate 637358-64-6P, Methyl 2-[[4-[2-[(methylsulfonyl)oxy]ethyl]phenoxy]methyl]benzoate 637358-65-7P, Methyl 2-[[4-[2-[4-(1H-imidazol-1-yl)phenoxy]ethyl]phenoxy]methyl]benzoate 637358-67-9P, Methyl

2-[[4-[2-[4-(benzyloxy)phenoxy]ethyl]phenoxy]methyl]benzoate  
 637358-69-1P, Methyl 2-[[4-[2-[4-[(methylsulfonyl)oxy]phenoxy]ethyl]  
 1]phenoxy]methyl]benzoate 637358-71-5P, Methyl  
 2-[[3-(2-hydroxyethyl)phenoxy]methyl]benzoate 637358-72-6P,  
 Methyl 2-[[3-[2-[4-(benzyloxy)phenoxy]ethyl]phenoxy]methyl]benzoat  
 e 637358-74-8P, Methyl 2-[[3-[2-(4-hydroxyphenoxy)ethyl]phenoxy]  
 methyl]benzoate 637358-75-9P, Methyl 2-[[3-[2-[4-  
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 637358-78-2P, Methyl 2-[[4-[3-[4-(benzyloxy)phenoxy]propyl]phenoxy]  
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 Methyl 2-[[4-[3-[4-[(methylsulfonyl)oxy]phenoxy]propyl]phenoxy]met  
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 hydroxyphenyl)propanamide 637358-85-1P, Methyl  
 2-[[4-[3-[[2-(2-ethoxyphenyl)ethyl]amino]-3-  
 oxopropyl]phenoxy]methyl]benzoate 637358-87-3P,  
 N-Ethyl-3-(4-hydroxyphenyl)-N-(2-(pyridin-2-yl)ethyl)propanamide  
 637358-88-4P, Methyl 2-[[4-[3-[ethyl(2-(pyridin-2-yl)ethyl)amino]-  
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 1-(2-Bromoethyl)-3-tert-butoxybenzene 637358-91-9P, Methyl  
 2-[[2-(3-tert-butoxyphenyl)ethyl]thio]benzoate 637358-92-0P,  
 Methyl 2-[[2-(3-hydroxyphenyl)ethyl]thio]benzoate 637358-93-1P,  
 N-Benzyl-2-bromo-N-hexylacetamide 637358-94-2P, Methyl  
 2-[[2-[3-[2-[benzyl(hexyl)amino]-2-oxoethoxy]phenyl]ethyl]thio]ben  
 zoate 637358-96-4P, N-[2-(2-Methoxyphenyl)ethyl]heptan-1-amine  
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 637358-99-7P, N-[2-(4-Chlorophenyl)ethyl]-N-heptylamine  
 637359-00-3P, Methyl 2-[[4-[2-[2-(4-chlorophenyl)ethyl](heptyl)am  
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 N-(2-Phenylethyl)heptan-1-amine 637359-03-6P, Methyl  
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 N-Ethyl-N-(2-fluorobenzyl)-2-(4-hydroxyphenoxy)acetamide  
 637359-06-9P, Methyl 2-[[4-[2-[ethyl(2-fluorobenzyl)amino]-2-  
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 2-[2-[4-[2-[isobutyl[4-(trifluoromethyl)benzyl]amino]-2-  
 oxoethoxy]phenyl]ethoxy]benzoate

(preparation of benzoic acid derivs. as modulators of PPAR- $\alpha$   
 and PPAR- $\gamma$ )

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE  
 FOR THIS RECORD. ALL CITATIONS AVAILABLE  
 IN THE RE FORMAT

L32 ANSWER 10 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:2678 HCAPLUS

DOCUMENT NUMBER: 140:59405

TITLE: Preparation of ortho-substituted benzoic acid  
 derivatives for the treatment of insulin  
 resistance

INVENTOR(S): Li, Lanna

PATENT ASSIGNEE(S): Astrazeneca AB, Swed.

SOURCE: PCT Int. Appl., 56 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004000294	A1	20031231	WO 2003-GB2591	2003 0617
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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EP 1517679	A1	20050330	EP 2003-732714	2003 0617
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BR 2003011839	A	20050405	BR 2003-11839	2003 0617
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JP 2005535618	T2	20051124	JP 2004-515008	2003 0617
NO 2004005223	A	20050317	NO 2004-5223	2004 1129
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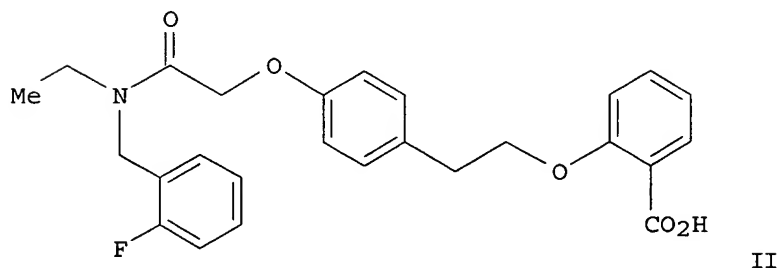
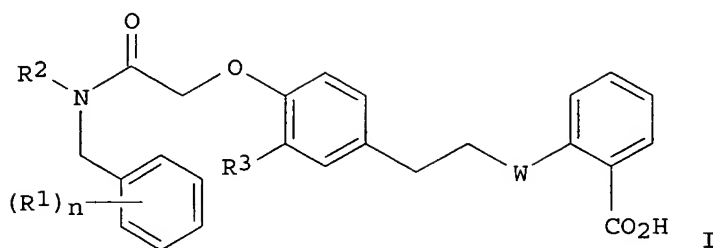
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OTHER SOURCE(S): MARPAT 140:59405  
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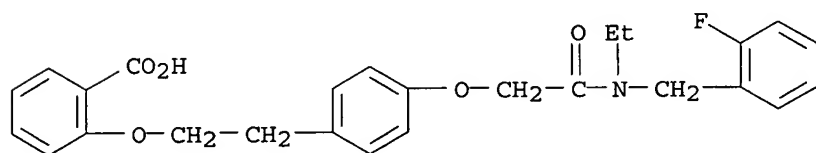
AB Title compds. I [ $n = 0-2$ ;  $R_1 = \text{halo, alkyl, alkoxy, etc.}$ ;  $R_2 = \text{alkyl}$ ;  $R_3 = \text{H, OCH}_3$ ;  $W = \text{O, S}$ ] are prepared. For instance, tert-Bu [4-(2-hydroxyethyl)phenoxy]acetate (preparation given) is sulfonylated ( $\text{CH}_2\text{Cl}_2$ ,  $\text{Et}_3\text{N}$ ,  $\text{MsCl}$ ), reacted with Me salicylate ( $\text{CH}_3\text{CN}$ ,  $\text{K}_2\text{CO}_3$ , reflux, 16 h), deprotected ( $\text{CH}_2\text{Cl}_2$ , TFA), coupled to N-(2-Fluorobenzyl)ethanamine and saponified to give II. Example compds. have an  $\text{EC}_{50} < 50 \mu\text{mol/L}$  for PPAR- $\alpha$ . I are useful in treating clin. conditions associated with insulin resistance.

IT **637763-49-6P**, 2-[2-[4-[2-[Ethyl(2-fluorobenzyl)amino]-2-oxoethoxy]phenyl]ethoxy]benzoic acid **637763-60-1P**, 2-[2-[4-[2-[(2,4-Difluorobenzyl)(heptyl)amino]-2-oxoethoxy]-3-methoxyphenyl]ethoxy]benzoic acid **637763-69-0P**, 2-[2-[4-[2-[(4-Chlorobenzyl)(ethyl)amino]-2-

oxoethoxy]phenyl]ethyl]thio]benzoic acid 637763-75-8P,  
 2-[[2-[4-[2-[Ethyl[4-(trifluoromethyl)benzyl]amino]-2-oxoethoxy]phenyl]ethyl]thio]benzoic acid 637763-77-0P,  
 2-[2-[4-[2-[Butyl[2-fluoro-4-(trifluoromethyl)benzyl]amino]-2-oxoethoxy]phenyl]ethoxy]benzoic acid 637763-79-2P,  
 2-[2-[4-[2-[(2,4-Difluorobenzyl)(propyl)amino]-2-oxoethoxy]phenyl]ethoxy]benzoic acid 637763-81-6P,  
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 2-[2-[4-[2-[(4-tert-Butylbenzyl)(ethyl)amino]-2-oxoethoxy]phenyl]ethoxy]benzoic acid 637763-87-2P,  
 2-[2-[4-[2-[Ethyl(4-fluorobenzyl)amino]-2-oxoethoxy]phenyl]ethoxy]benzoic acid 637763-89-4P,  
 2-[[2-[4-[2-[Ethyl(2-fluorobenzyl)amino]-2-oxoethoxy]phenyl]ethyl]thio]benzoic acid 637763-92-9P,  
 2-[[2-[4-[2-[(2-Chlorobenzyl)(ethyl)amino]-2-oxoethoxy]phenyl]ethyl]thio]benzoic acid 637763-93-0P,  
 2-[2-[4-[2-[(4-Chlorobenzyl)(ethyl)amino]-2-oxoethoxy]phenyl]ethoxy]benzoic acid 637763-94-1P,  
 2-[2-[4-[2-[Ethyl(4-trifluoromethylbenzyl)amino]-2-oxoethoxy]phenyl]ethoxy]benzoic acid  
 (preparation of ortho-substituted benzoic acid derivs. for treatment of insulin resistance)

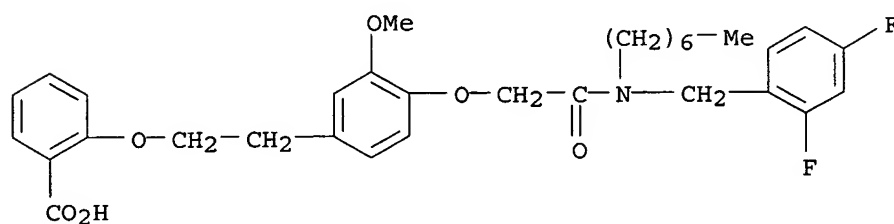
RN 637763-49-6 HCAPLUS

CN Benzoic acid, 2-[2-[4-[2-[ethyl[(2-fluorophenyl)methyl]amino]-2-oxoethoxy]phenyl]ethoxy]- (9CI) (CA INDEX NAME)



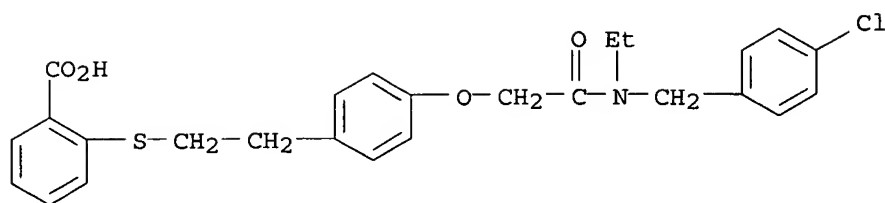
RN 637763-60-1 HCAPLUS

CN Benzoic acid, 2-[2-[4-[2-[[2,4-difluorophenyl)methyl]heptylamino]-2-oxoethoxy]-3-methoxyphenyl]ethoxy]- (9CI) (CA INDEX NAME)



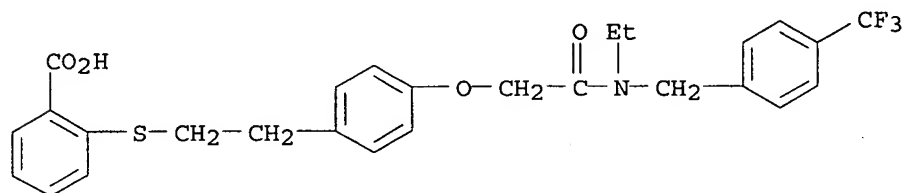
RN 637763-69-0 HCAPLUS

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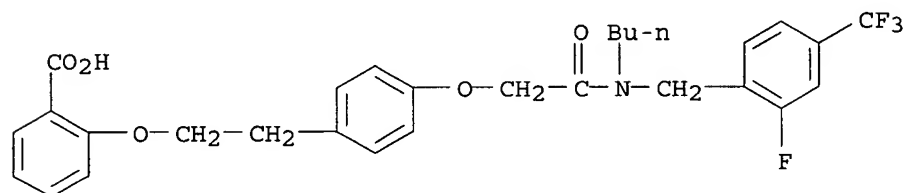
RN 637763-75-8 HCAPLUS

CN Benzoic acid, 2-[[2-[4-[2-[ethyl[[4-(trifluoromethyl)phenyl]methyl]amino]-2-oxoethoxy]phenyl]ethyl]thio]- (9CI) (CA INDEX NAME)



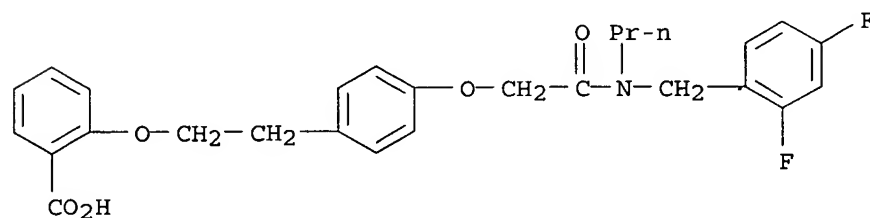
RN 637763-77-0 HCAPLUS

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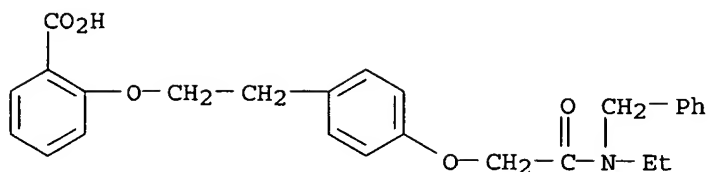
RN 637763-79-2 HCAPLUS

CN Benzoic acid, 2-[2-[4-[2-[[2,4-difluorophenyl]methyl]propylamino]-2-oxoethoxy]phenyl]ethoxy]- (9CI) (CA INDEX NAME)



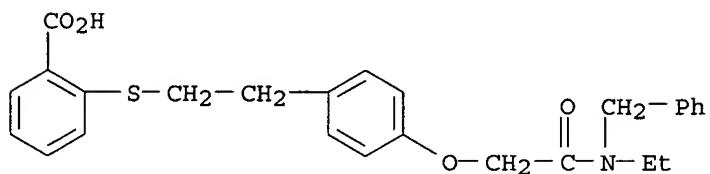
RN 637763-81-6 HCAPLUS

CN Benzoic acid, 2-[2-[4-[2-[ethyl(phenylmethyl)amino]-2-oxoethoxy]phenyl]ethoxy]- (9CI) (CA INDEX NAME)



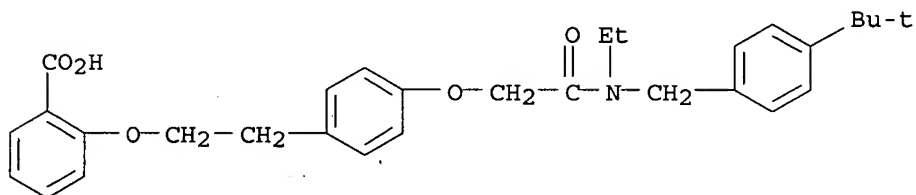
RN 637763-83-8 HCAPLUS

CN Benzoic acid, 2-[[2-[4-[2-[ethyl(phenylmethyl)amino]-2-oxoethoxy]phenyl]ethyl]thio]- (9CI) (CA INDEX NAME)



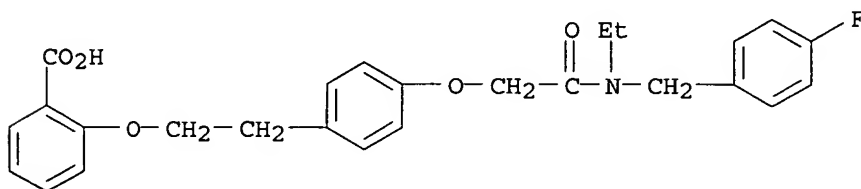
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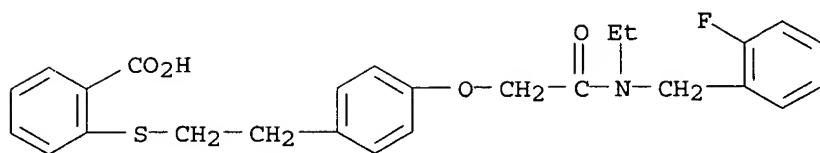
RN 637763-87-2 HCAPLUS

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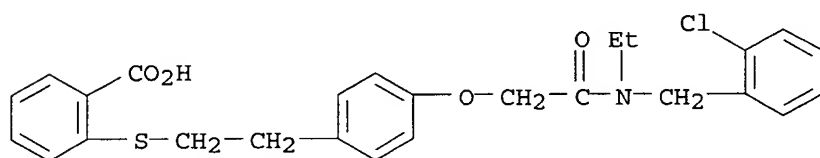
RN 637763-89-4 HCAPLUS

CN Benzoic acid, 2-[[2-[4-[2-[ethyl[(2-fluorophenyl)methyl]amino]-2-oxoethoxy]phenyl]ethyl]thio]- (9CI) (CA INDEX NAME)



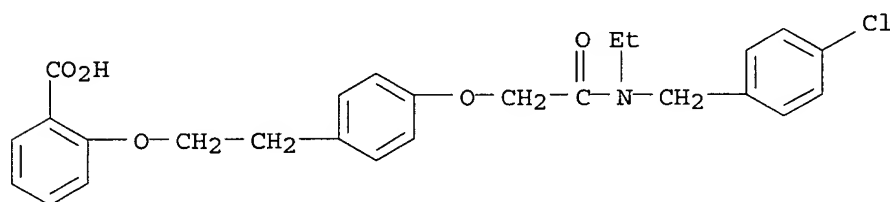
RN 637763-92-9 HCAPLUS

CN Benzoic acid, 2-[[2-[4-[2-[[2-(2-chlorophenyl)methyl]ethylamino]-2-oxoethoxy]phenyl]ethyl]thio]- (9CI) (CA INDEX NAME)



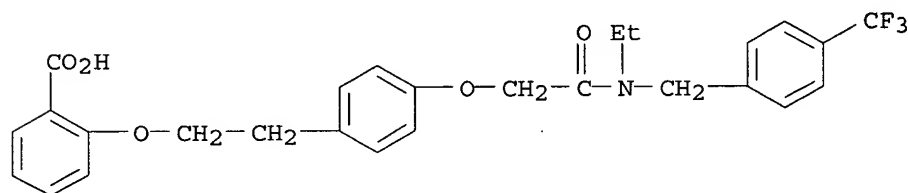
RN 637763-93-0 HCAPLUS

CN Benzoic acid, 2-[2-[4-[2-[[2-(4-chlorophenyl)methyl]ethylamino]-2-oxoethoxy]phenyl]ethoxy]- (9CI) (CA INDEX NAME)



RN 637763-94-1 HCAPLUS

CN Benzoic acid, 2-[2-[4-[2-[ethyl[[4-(trifluoromethyl)phenyl]methyl]amino]-2-oxoethoxy]phenyl]ethoxy]- (9CI) (CA INDEX NAME)

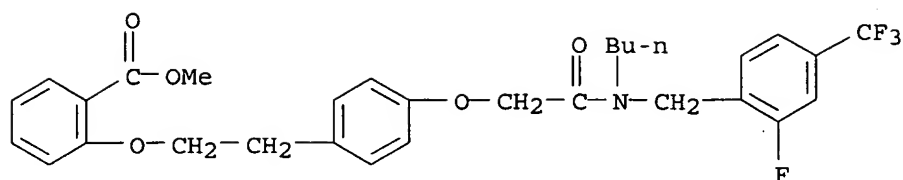


IT 637763-76-9, Methyl 2-[2-[4-[2-[butyl[2-fluoro-4-(trifluoromethyl)benzyl]amino]-2-oxoethoxy]phenyl]ethoxy]benzoate (preparation of ortho-substituted benzoic acid derivs. for treatment of insulin resistance)

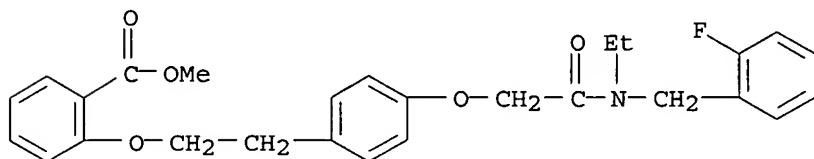
RN 637763-76-9 HCAPLUS

CN Benzoic acid, 2-[2-[4-[2-[butyl[[2-fluoro-4-(trifluoromethyl)phenyl]methyl]amino]-2-oxoethoxy]phenyl]ethoxy]-, methyl ester (9CI) (CA INDEX NAME)

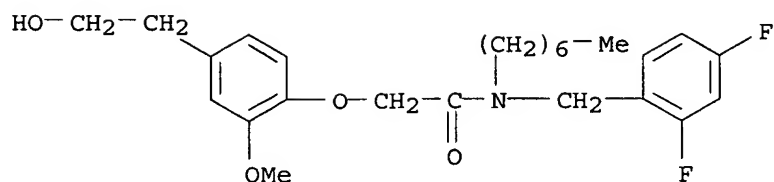




- IT 637763-47-4P, Methyl 2-[2-[4-[2-[ethyl(2-fluorobenzyl)amino]-2-oxoethoxy]phenyl]ethoxy]benzoate  
 637763-54-3P, N-(2,4-Difluorobenzyl)-N-heptyl-2-[4-(2-hydroxyethyl)-2-methoxyphenoxy]acetamide 637763-56-5P,  
 2-[4-[2-[(2,4-Difluorobenzyl)(heptyl)amino]-2-oxoethoxy]-3-methoxyphenyl]ethyl methanesulfonate 637763-58-7P,  
 Methyl 2-[2-[4-[2-[(2,4-difluorobenzyl)(heptyl)amino]-2-oxoethoxy]-3-methoxyphenyl]ethoxy]benzoate 637763-67-8P, Methyl  
 2-[[2-[4-[2-[(4-chlorobenzyl)(ethyl)amino]-2-oxoethoxy]phenyl]ethyl]thio]benzoate 637763-73-6P,  
 Methyl 2-[[2-[4-[2-[ethyl(4-(trifluoromethyl)benzyl)amino]-2-oxoethoxy]phenyl]ethyl]thio]benzoate 637763-78-1P,  
 Methyl 2-[2-[4-[2-[(2,4-difluorobenzyl)(propyl)amino]-2-oxoethoxy]phenyl]ethoxy]benzoate 637763-80-5P, Methyl  
 2-[2-[4-[2-[benzyl(ethyl)amino]-2-oxoethoxy]phenyl]ethoxy]benzoate 637763-82-7P, Methyl 2-[[2-[4-[2-[benzyl(ethyl)amino]-2-oxoethoxy]phenyl]ethyl]thio]benzoate 637763-84-9P,  
 Methyl 2-[2-[4-[2-[(4-tert-butylbenzyl)(ethyl)amino]-2-oxoethoxy]phenyl]ethoxy]benzoate 637763-86-1P, Methyl  
 2-[2-[4-[2-[ethyl(4-fluorobenzyl)amino]-2-oxoethoxy]phenyl]ethoxy]benzoate 637763-88-3P, Methyl  
 2-[[2-[4-[2-[benzyl(2-fluorobenzyl)amino]-2-oxoethoxy]phenyl]ethyl]thio]benzoate 637763-91-8P,  
 Methyl 2-[[2-[4-[2-[(2-chlorobenzyl)(ethyl)amino]-2-oxoethoxy]phenyl]ethyl]thio]benzoate  
 (preparation of ortho-substituted benzoic acid derivs. for treatment of insulin resistance)
- RN 637763-47-4 HCAPLUS  
 CN Benzoic acid, 2-[2-[4-[2-[ethyl[(2-fluorophenyl)methyl]amino]-2-oxoethoxy]phenyl]ethoxy]-, methyl ester (9CI). (CA INDEX NAME)

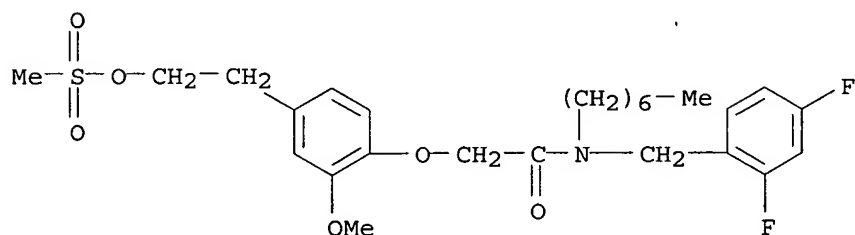


- RN 637763-54-3 HCAPLUS  
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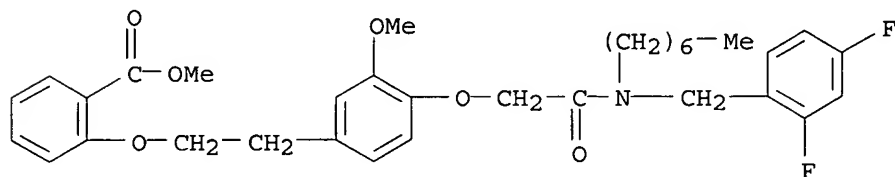
RN 637763-56-5 HCAPLUS

CN Acetamide, N-[(2,4-difluorophenyl)methyl]-N-heptyl-2-[2-methoxy-4-[(2-hydroxyethyl)oxy]phenyl]- (9CI) (CA INDEX NAME)



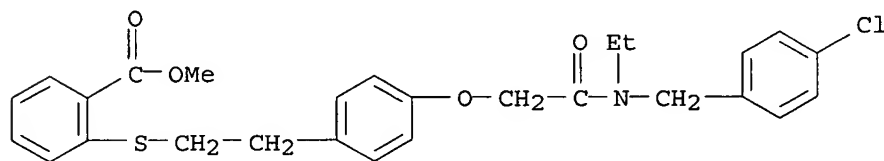
RN 637763-58-7 HCAPLUS

CN Benzoic acid, 2-[2-[4-[2-[(2,4-difluorophenyl)methyl]heptylamino]-2-oxoethoxy]-3-methoxyphenyl]ethoxy]-, methyl ester (9CI) (CA INDEX NAME)



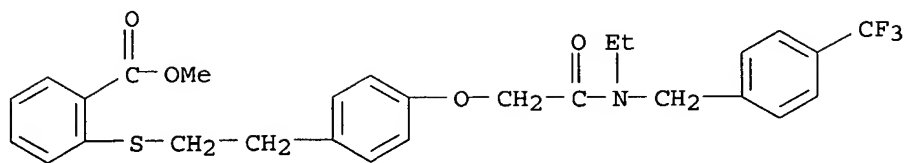
RN 637763-67-8 HCAPLUS

CN Benzoic acid, 2-[2-[4-[2-[(4-chlorophenyl)methyl]ethylamino]-2-oxoethoxy]phenyl]ethylthio]-, methyl ester (9CI) (CA INDEX NAME)

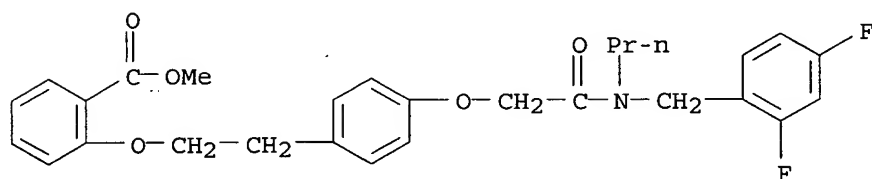


RN 637763-73-6 HCAPLUS

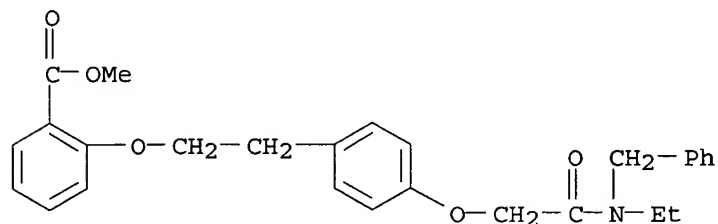
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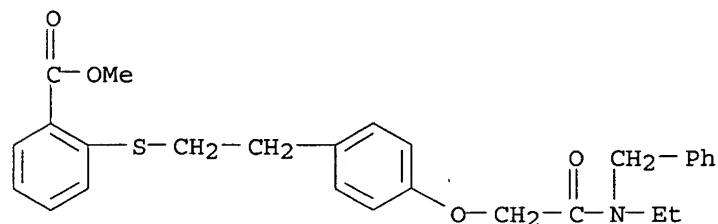
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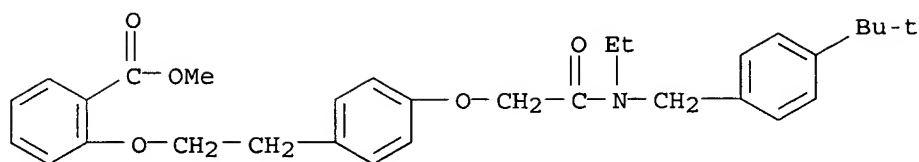
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 CN Benzoic acid, 2-[2-[4-[2-[ethyl(phenylmethyl)amino]-2-oxoethoxy]phenyl]ethoxy]-, methyl ester (9CI) (CA INDEX NAME)



RN 637763-82-7 HCAPLUS  
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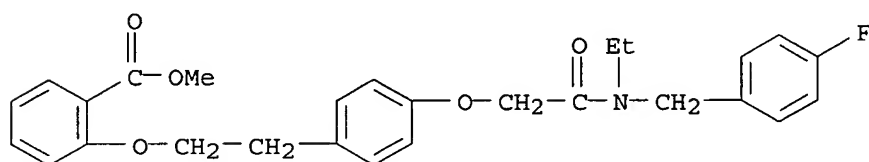


RN 637763-84-9 HCAPLUS  
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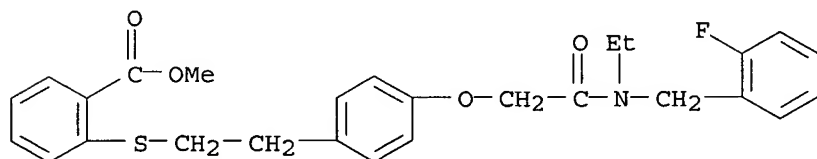
RN 637763-86-1 HCAPLUS

CN Benzoic acid, 2-[2-[4-[2-[ethyl[(4-fluorophenyl)methyl]amino]-2-oxoethoxy]phenyl]ethoxy]-, methyl ester (9CI) (CA INDEX NAME)



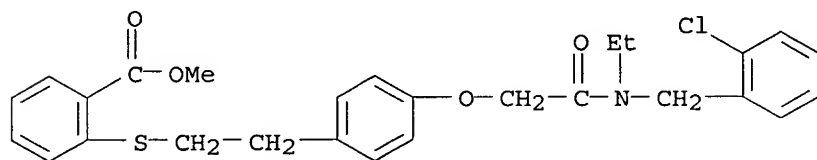
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CN Benzoic acid, 2-[2-[4-[2-[ethyl[(2-fluorophenyl)methyl]amino]-2-oxoethoxy]phenyl]ethylthio]-, methyl ester (9CI) (CA INDEX NAME)



RN 637763-91-8 HCAPLUS

CN Benzoic acid, 2-[2-[4-[2-[ethyl[(2-chlorophenyl)methyl]ethylamino]-2-oxoethoxy]phenyl]ethylthio]-, methyl ester (9CI) (CA INDEX NAME)



IC ICM A61K031-19

ICS A61P003-06; A61P003-10; C07C323-62; C07C235-20

CC 25-17 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)

Section cross-reference(s): 1, 63

IT Anticholesteremic agents

Antidiabetic agents

Antihypertensives

Antiobesity agents

(combination pharmaceutical; preparation of ortho-substituted benzoic acid derivs. for treatment of insulin resistance)

IT Peroxisome proliferator-activated receptors

( $\alpha$ ; preparation of ortho-substituted benzoic acid derivs. for treatment of insulin resistance)

- IT 637763-49-6P, 2-[2-[4-[2-[Ethyl(2-fluorobenzyl)amino]-2-oxoethoxy]phenyl]ethoxy]benzoic acid 637763-60-1P,  
2-[2-[4-[2-[(2,4-Difluorobenzyl)(heptyl)amino]-2-oxoethoxy]-3-methoxyphenyl]ethoxy]benzoic acid 637763-69-0P,  
2-[2-[4-[2-[(4-Chlorobenzyl)(ethyl)amino]-2-oxoethoxy]phenyl]ethyl]thio]benzoic acid 637763-75-8P,  
2-[2-[4-[2-[Ethyl[4-(trifluoromethyl)benzyl]amino]-2-oxoethoxy]phenyl]ethyl]thio]benzoic acid 637763-77-0P,  
2-[2-[4-[2-[Butyl[2-fluoro-4-(trifluoromethyl)benzyl]amino]-2-oxoethoxy]phenyl]ethoxy]benzoic acid 637763-79-2P,  
2-[2-[4-[2-[(2,4-Difluorobenzyl)(propyl)amino]-2-oxoethoxy]phenyl]ethoxy]benzoic acid 637763-81-6P,  
2-[2-[4-[2-[Benzyl(ethyl)amino]-2-oxoethoxy]phenyl]ethoxy]benzoic acid 637763-83-8P, 2-[2-[4-[2-[Benzyl(ethyl)amino]-2-oxoethoxy]phenyl]ethyl]thio]benzoic acid 637763-85-0P,  
2-[2-[4-[2-[(4-tert-Butylbenzyl)(ethyl)amino]-2-oxoethoxy]phenyl]ethoxy]benzoic acid 637763-87-2P,  
2-[2-[4-[2-[Ethyl(4-fluorobenzyl)amino]-2-oxoethoxy]phenyl]ethoxy]benzoic acid 637763-89-4P,  
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2-[2-[4-[2-[(2-Chlorobenzyl)(ethyl)amino]-2-oxoethoxy]phenyl]ethyl]thio]benzoic acid 637763-93-0P,  
2-[2-[4-[2-[(4-Chlorobenzyl)(ethyl)amino]-2-oxoethoxy]phenyl]ethoxy]benzoic acid 637763-94-1P,  
2-[2-[4-[2-[Ethyl(4-trifluoromethylbenzyl)amino]-2-oxoethoxy]phenyl]ethoxy]benzoic acid  
(preparation of ortho-substituted benzoic acid derivs. for treatment of insulin resistance)
- IT 104-86-9, 1-(4-Chlorophenyl)methanamine 119-36-8, Methyl salicylate 140-75-0, 1-(4-Fluorophenyl)methanamine 501-94-0, 4-(2-Hydroxyethyl)phenol 3300-51-4, 1-[4-(Trifluoromethyl)phenyl]methanamine 4892-02-8, Methyl 2-mercaptobenzoate 5292-43-3, tert-Butyl bromoacetate 14321-27-8, N-Benzyl-N-ethylamine 22118-09-8, Bromoacetyl chloride 62924-61-2, N-(2-Chlorobenzyl)-N-ethylamine 64567-25-5, N-(2-Fluorobenzyl)ethanamine 152821-50-6, N-(4-tert-Butylbenzyl)-N-ethylamine 637014-99-4, N-(2,4-Difluorobenzyl)-N-heptylamine 637015-27-1, N-(2,4-Difluorobenzyl)-N-propylamine 637359-16-1, Methyl 2-[2-[4-(2-chloro-2-oxoethoxy)phenyl]ethoxy]benzoate 637763-76-9, Methyl 2-[2-[4-[2-[butyl[2-fluoro-4-(trifluoromethyl)benzyl]amino]-2-oxoethoxy]phenyl]ethoxy]benzoate  
(preparation of ortho-substituted benzoic acid derivs. for treatment of insulin resistance)
- IT 57058-33-0P, N-(4-Chlorobenzyl)acetamide 69957-83-1P, N-(4-Chlorobenzyl)-N-ethylamine 86010-68-6P, N-(4-Fluorobenzyl)acetamide 90390-12-8P, N-[4-(Trifluoromethyl)benzyl]ethanamine 119293-44-6P, tert-Butyl [4-(2-hydroxyethyl)phenoxy]acetate 162401-03-8P, N-(4-Fluorobenzyl)ethanamine 637763-42-9P, tert-Butyl [4-[2-[(methylsulfonyl)oxy]ethyl]phenoxy]acetate 637763-43-0P, Methyl 2-[2-[4-(2-tert-butoxy-2-oxoethoxy)phenyl]ethoxy]benzoate 637763-45-2P, [4-[2-[2-(Methoxycarbonyl)phenoxy]ethyl]phenoxy]acetic acid 637763-47-4P, Methyl 2-[2-[4-[2-[ethyl(2-fluorobenzyl)amino]-2-oxoethoxy]phenyl]ethoxy]benzoate 637763-51-0P, 2-Bromo-N-(2,4-difluorobenzyl)-N-heptylacetamide 637763-54-3P, N-(2,4-Difluorobenzyl)-N-heptyl-2-[4-(2-

hydroxyethyl)-2-methoxyphenoxy]acetamide 637763-56-5P,  
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 3-methoxyphenyl]ethoxy]benzoate 637763-63-4P, Methyl  
 2-[2-[4-(2-tert-butoxy-2-oxoethoxy)phenyl]ethyl]thio]benzoate  
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 oxoethoxy]phenyl]ethoxy]benzoate 637763-82-7P, Methyl  
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 fluorobenzyl)amino]-2-oxoethoxy]phenyl]ethyl]thio]benzoate  
 637763-91-8P, Methyl 2-[2-[4-[2-[(2-  
 chlorobenzyl)(ethyl)amino]-2-oxoethoxy]phenyl]ethyl]thio]benzoate  
 (preparation of ortho-substituted benzoic acid derivs. for treatment  
 of insulin resistance)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE  
 FOR THIS RECORD. ALL CITATIONS AVAILABLE  
 IN THE RE FORMAT

L32 ANSWER 11 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2003:491169 HCAPLUS  
 DOCUMENT NUMBER: 139:69054  
 TITLE: Preparation of substituted phenylpropionic  
 acid derivatives as agonists to human  
 peroxisome proliferator-activated  
 receptor alpha (PPAR)  
 INVENTOR(S): Alstermark Lindstedt, Eva-Lotte; Olsson, Anna  
 Christina; Li, Lanna  
 PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited  
 SOURCE: PCT Int. Appl., 43 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 5  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003051822	A1	20030626	WO 2002-GB5744	2002 1218

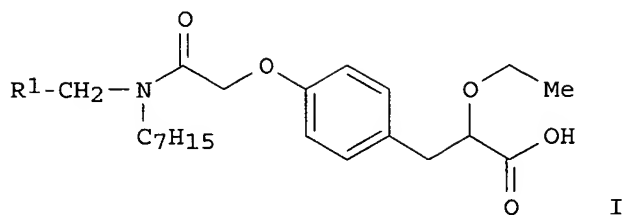
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 GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG,  
 KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK,  
 MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD,

SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ,  
VC, VN, YU, ZA, ZM, ZW  
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM,  
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DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT,  
SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW,  
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PRIORITY APPLN. INFO.:	SE 2001-4334	A	
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	WO 2003-GB305602	A	
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	WO 2004-EP6597	A	
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			0617
	US 2005-499261	A2	
			2005
			0304

OTHER SOURCE(S): MARPAT 139:69054  
GI



AB The present invention provides the S enantiomer of a compound of formula (I) (wherein R1 represents 2,4-difluorophenyl or cyclohexyl) as well as pharmaceutically acceptable salts, solvates, crystalline forms and prodrugs thereof, processes for preparing such compds., their the utility in treating clin. conditions including lipid disorders (dyslipidemias) whether or not associated with insulin resistance, methods for their therapeutic use, and



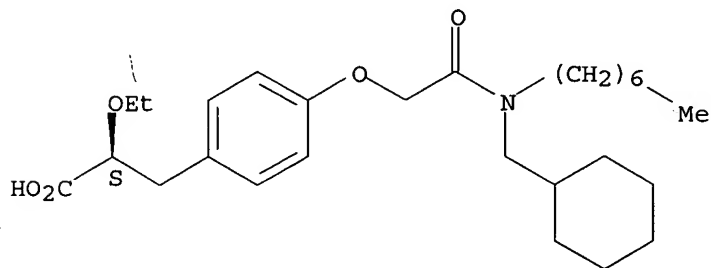
pharmaceutical compns. containing them. Thus, to a solution of [4-((2S)-2,3-diethoxy-3-oxopropyl)phenoxy]acetic acid (0.108 g) 3.6 mL CH<sub>2</sub>Cl<sub>2</sub> were added N-(cyclohexylmethyl)-N-heptylamine hydrochloride (0.090 g) and DMAP (0.098 g) followed by 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (0.070 g) and the reaction mixture was stirred at room temperature overnight to give, after workup and silica gel chromatog., Et (2S)-3-[4-[2-[(cyclohexylmethyl)(heptyl)amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoate which (0.031 g) was saponified with LiOH in aqueous THF at room temperature overnight and acidified with aqueous 2 M HCl to give (2S)-3-[4-[2-[(cyclohexylmethyl)(heptyl)amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoic acid. The compds. I had EC<sub>50</sub> of less than 0.5 μmol/L for PPARα and preferred compds. have EC<sub>50</sub> of less than 0.05 μmol/L for PPARα. They were more potent with respect to PPARα than with respect to PPARγ.

IT 549501-66-8P, (2S)-3-[4-[2-[(Cyclohexylmethyl)(heptyl)amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoic acid 549501-72-6P, (2S)-3-[4-[2-[(2,4-Difluorobenzyl)(heptyl)amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoic acid (preparation of substituted phenylpropionic acid derivs. as agonists to human **peroxisome** proliferator-activated receptor alpha (PPAR) for treating lipid disorders)

RN 549501-66-8 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[(cyclohexylmethyl)heptylamino]-2-oxoethoxy]-α-ethoxy-, (αS)- (9CI) (CA INDEX NAME)

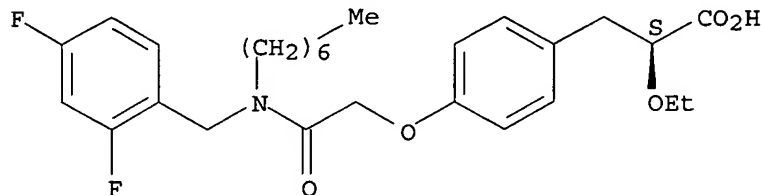
Absolute stereochemistry.



RN 549501-72-6 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[(2,4-difluorophenyl)methyl]heptylamino]-2-oxoethoxy]-α-ethoxy-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IC ICM C07C235-20

ICS A61K031-16; A61P003-00

CC 25-18 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)

## Section cross-reference(s): 1

- ST phenylpropionic acid prepn agonist human **peroxisome** proliferator activated receptor; lipid disorder dyslipidemia treatment phenylpropionic acid prepn
- IT Human  
(preparation of substituted phenylpropionic acid derivs. as agonists to human **peroxisome** proliferator-activated receptor alpha (PPAR) for treating lipid disorders)
- IT Dyslipidemia  
(preparation of substituted phenylpropionic acid derivs. as agonists to human **peroxisome** proliferator-activated receptor alpha (PPAR) for treating lipid disorders)
- IT **Peroxisome** proliferator-activated receptors  
( $\alpha$ ; preparation of substituted phenylpropionic acid derivs. as agonists to human **peroxisome** proliferator-activated receptor alpha (PPAR) for treating lipid disorders)
- IT 134523-00-5, Atorvastatin 287714-41-4, Rosuvastatin  
(drug containing; preparation of substituted phenylpropionic acid derivs. as agonists to human **peroxisome** proliferator-activated receptor alpha (PPAR) for treating lipid disorders)
- IT 439087-18-0 439087-21-5 439087-31-7 439087-34-0  
439087-36-2 439087-37-3 439087-38-4 439087-48-6  
439087-61-3 439087-63-5 439087-88-4 439087-89-5  
439087-96-4 439088-00-3 439088-01-4 439088-02-5  
439088-03-6 501692-15-5 501692-16-6 501692-17-7  
501692-21-3 501692-27-9 501692-28-0 501692-40-6  
501692-41-7 501692-43-9 501692-44-0 501692-46-2  
501692-50-8 549501-76-0 549501-77-1 549501-78-2  
549501-79-3 549501-80-6 549501-81-7 549501-82-8  
549501-83-9 549501-84-0  
(ideal bile acid transport system (IBAT) inhibitor, drug containing; preparation of substituted phenylpropionic acid derivs. as agonists to human **peroxisome** proliferator-activated receptor alpha (PPAR) for treating lipid disorders)
- IT 549501-67-9P, Ethyl (2S)-3-[4-[2-(benzyloxy)-2-oxoethoxy]phenyl]-2-ethoxypropanoate 549501-68-0P, [4-[(2S)-2,3-Diethoxy-3-oxopropyl]phenoxy]acetic acid 549501-69-1P, N-(Cyclohexylmethyl)heptanamide 549501-70-4P, N-(Cyclohexylmethyl)-N-heptylamine hydrochloride 549501-71-5P, Ethyl (2S)-3-[4-[2-[(cyclohexylmethyl)(heptyl)amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoate 549501-73-7P, N-(2,4-Difluorobenzyl)heptanamide 549501-74-8P 549501-75-9P, Ethyl (2S)-3-[4-[2-[(2,4-difluorobenzyl)(heptyl)amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoate  
(intermediate; preparation of substituted phenylpropionic acid derivs. as agonists to human **peroxisome** proliferator-activated receptor alpha (PPAR) for treating lipid disorders)
- IT 549501-66-8P, (2S)-3-[4-[2-[(Cyclohexylmethyl)(heptyl)amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoic acid 549501-72-6P, (2S)-3-[4-[2-[(2,4-Difluorobenzyl)(heptyl)amino]-2-oxoethoxy]phenyl]-2-ethoxypropanoic acid  
(preparation of substituted phenylpropionic acid derivs. as agonists to human **peroxisome** proliferator-activated receptor alpha (PPAR) for treating lipid disorders)
- IT 111-14-8, n-Heptanoic acid 3218-02-8, Aminomethylcyclohexane 5437-45-6, Benzyl bromoacetate 72235-52-0, 2,4-Difluorobenzylamine 222555-06-8, Ethyl (2S)-2-ethoxy-3-(4-hydroxyphenyl)propanoate

(reactant; preparation of substituted phenylpropionic acid derivs.  
as agonists to human **peroxisome** proliferator-  
activated receptor alpha (PPAR) for treating lipid disorders)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE  
FOR THIS RECORD. ALL CITATIONS AVAILABLE  
IN THE RE FORMAT

L32 ANSWER 12 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:491168 HCAPLUS

DOCUMENT NUMBER: 139:69049

TITLE: Preparation of substituted phenylpropionic  
acid derivatives as agonists to human  
**peroxisome** proliferator-activated  
receptor alpha (PPAR)

INVENTOR(S): Alstermark Lindstedt, Eva-Lotte; Olsson, Anna  
Christina; Li, Lanna

PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited

SOURCE: PCT Int. Appl., 40 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 5

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003051821	A1	20030626	WO 2002-GB5738	2002 1218

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GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG,  
KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK,  
MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD,  
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VC, VN, YU, ZA, ZM, ZW

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DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT,  
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CA 2470491	AA	20030626	CA 2002-2470491	2002 1218
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AU 2002366315	A1	20030630	AU 2002-366315	2002 1218
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EP 1458673	A1	20040922	EP 2002-804964	2002 1218
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WO 2004-EP6597

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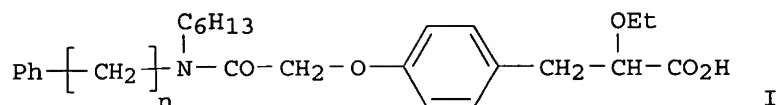
2004  
0617

US 2005-499261

A2

2005  
0304OTHER SOURCE(S):  
GI

MARPAT 139:69049



AB The S enantiomer of I, n = 1 or 2, (C<sub>6</sub>H<sub>13</sub> = hexyl) as well as their pharmaceutically acceptable salts, solvates, crystalline forms and prodrugs are synthesized using various solvents and in presence of charcoal-supported palladium catalyst. The utility of these compds. in clin. conditions such as lipid disorders (dyslipidemias) whether or not associated with insulin resistance and therapeutic and other pharmaceutical activities is also investigated. For example, (2S)-3-(4{2-[benzyl(hexyl)amino]-2-oxoethoxy}phenyl)2-ethoxypropionic acid was prepared in 58% yield via reaction of (2S)-2-ethoxy-3-(4-hydroxyphenyl)propanoate and benzyl bromoacetate.

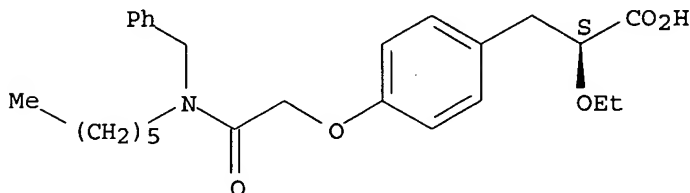
IT 549532-33-4P 549532-35-6P

(preparation of enantiomeric substituted phenylpropionic acid derivs. as agonists to human **peroxisome** proliferator-activated receptor)

RN 549532-33-4 HCAPLUS

CN Benzenepropanoic acid, α-ethoxy-4-[2-[hexyl(phenylmethyl)amino]-2-oxoethoxy]-, (αS)- (9CI) (CA INDEX NAME)

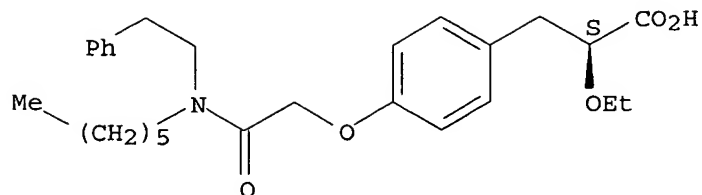
Absolute stereochemistry.



RN 549532-35-6 HCAPLUS

CN Benzenepropanoic acid, α-ethoxy-4-[2-[hexyl(2-phenylethyl)amino]-2-oxoethoxy]-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



- IC ICM C07C235-20  
ICS A61K031-16; A61P003-00
- CC 25-17 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)  
Section cross-reference(s): 1, 63
- ST substituted phenylpropionic acid deriv enantiomer deriv prepn  
agonist activity; human **peroxisome** proliferator  
activated receptor substituted phenylpropionic acid deriv; PPAR  
receptor substituted phenylpropionic acid deriv enantiomer
- IT Antiarteriosclerotics  
(antiatherosclerotics; preparation of enantiomeric substituted  
phenylpropionic acid derivs. as agonists to human  
**peroxisome** proliferator-activated receptor)
- IT Structure-activity relationship  
(hydroxymethylglutaryl CoA reductase-inhibiting; preparation of  
enantiomeric substituted phenylpropionic acid derivs. as  
agonists to human **peroxisome** proliferator-activated  
receptor)
- IT Bile acids  
(ileal bile acid transport, inhibitor; preparation of enantiomeric  
substituted phenylpropionic acid derivs. as agonists to human  
**peroxisome** proliferator-activated receptor)
- IT Charcoal  
(palladium supported with; preparation of enantiomeric substituted  
phenylpropionic acid derivs. as agonists to human  
**peroxisome** proliferator-activated receptor)
- IT Anticholesteremic agents  
Antidiabetic agents  
Antihypertensives  
Antiobesity agents  
Human  
Hypolipemic agents  
(preparation of enantiomeric substituted phenylpropionic acid  
derivs. as agonists to human **peroxisome**  
proliferator-activated receptor)
- IT **Peroxisome** proliferator-activated receptors  
(preparation of enantiomeric substituted phenylpropionic acid  
derivs. as agonists to human **peroxisome**  
proliferator-activated receptor)
- IT Drug delivery systems  
(prodrugs; preparation of enantiomeric substituted phenylpropionic  
acid derivs. as agonists to human **peroxisome**  
proliferator-activated receptor)
- IT 7440-05-3, Palladium, uses  
(charcoal-supported; preparation of enantiomeric substituted  
phenylpropionic acid derivs. as agonists to human  
**peroxisome** proliferator-activated receptor)
- IT 37250-24-1P, HMG-CoA reductase  
(inhibitors; preparation of enantiomeric substituted phenylpropionic  
acid derivs. as agonists to human **peroxisome**  
proliferator-activated receptor)

IT 439087-18-0P 439087-21-5P 439087-27-1P 439087-31-7P  
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 549501-83-9P 549501-84-0P 549532-33-4P  
 549532-35-6P 549532-37-8P  
 (preparation of enantiomeric substituted phenylpropionic acid  
 derivs. as agonists to human **peroxisome**  
 proliferator-activated receptor)

IT 5437-45-6, Benzyl bromoacetate 24997-83-9, N-Hexyl-2-  
 phenylethylamine 25468-44-4, N-Hexylbenzylamine 25952-53-8,  
 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride  
 222555-06-8  
 (preparation of enantiomeric substituted phenylpropionic acid  
 derivs. as agonists to human **peroxisome**  
 proliferator-activated receptor)

IT 549501-67-9P 549501-68-0P 549532-34-5P 549532-36-7P  
 (preparation of enantiomeric substituted phenylpropionic acid  
 derivs. as agonists to human **peroxisome**  
 proliferator-activated receptor)

IT 67-68-5, DMSO, uses 109-99-9, THF, uses 57951-36-7,  
 Dimethylaminopyridine  
 (solvent; preparation of enantiomeric substituted phenylpropionic  
 acid derivs. as agonists to human **peroxisome**  
 proliferator-activated receptor)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE  
 FOR THIS RECORD. ALL CITATIONS AVAILABLE  
 IN THE RE FORMAT

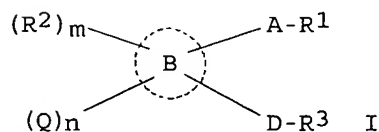
L32 ANSWER 13 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2003:154382 HCAPLUS  
 DOCUMENT NUMBER: 138:187795  
 TITLE: Preparation of aryl or heterocyclyl-  
 substituted benzoic acid and alkanolic acid  
 derivatives as antagonists of prostaglandin E2  
 (PEG2) receptors  
 INVENTOR(S): Tani, Kousuke; Asada, Masaki; Kobayashi,  
 Kaoru; Narita, Masami; Ogawa, Mikio  
 PATENT ASSIGNEE(S): Ono Pharmaceutical Co., Ltd., Japan  
 SOURCE: PCT Int. Appl., 1009 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2003016254	A1	20030227	WO 2002-JP8120	2002 0808

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GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG,  
 KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN,  
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 SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,  
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 BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE,  
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 WO 2002-JP8120 W 2002  
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 OTHER SOURCE(S): MARPAT 138:187795  
 GI





AB Carboxylic acid derivs. (I) and nontoxic salts thereof [wherein R1 = CO<sub>2</sub>H, CO<sub>2</sub>R<sub>4</sub>, CH<sub>2</sub>OH, COR<sub>5</sub>SO<sub>2</sub>R<sub>6</sub>, CONH<sub>2</sub>, CH<sub>2</sub>NR<sub>5</sub>SO<sub>2</sub>R<sub>6</sub>, CH<sub>2</sub>NR<sub>9</sub>COR<sub>10</sub>, CH<sub>2</sub>NR<sub>9</sub>CONR<sub>5</sub>SO<sub>2</sub>R<sub>6</sub>, CH<sub>2</sub>SO<sub>2</sub>NR<sub>9</sub>COR<sub>10</sub>, CH<sub>2</sub>O<sub>2</sub>CNR<sub>5</sub>SO<sub>2</sub>R<sub>6</sub>, tetrazole, 1,2,4-oxadiazol-5-one, 1,2,4-oxadiazol-5-thione, 1,2,4-thiadiazol-5-one, etc. (wherein R<sub>4</sub> = C1-6 alkyl, hydroxy-C1-4 alkyl, C1-4 alkoxy-C1-4 alkyl, carboxy-C1-4 alkyl, etc.; R<sub>5</sub>, R<sub>9</sub> = H, C1-6 alkyl; R<sub>6</sub> = C1-6 alkyl, C3-15 mono-, di-, or tricarboxylic, 3- to 13-membered mono-, di-, or tricyclic heterocyclyl, etc.; R<sub>10</sub> = H, R<sub>6</sub>); A = a single bond, C1-6 alkylene, C2-6 alkenylene, C2-6 alkynylene, etc.; the ring B = C3-12 mono- or dicyclic carbocyclic ring, 3- to 12-membered mono- or dicyclic heterocyclic ring; R<sub>2</sub> = C1-6 alkyl, C1-6 alkoxy, C1-6 alkylthio, C2-6 alkenyl, C2-6 alkynyl, halo, CHF<sub>2</sub>, CF<sub>3</sub>, NO<sub>2</sub>, cyano, Ph, oxo; m, n = 0,1,2; Q = (C1-4 alkylene, C2-4 alkenylene, or C2-4 alkynylene)-Cyc<sub>2</sub>, -C1-4 alkylene-Z-Cyc<sub>3</sub>, amino-C1-4 alkyl, cyano-C1-4 alkyl, acylamino-C1-4 alkyl, 3- to 7-membered monocyclic carbocyclyl, 3- to 6-membered monocyclic heterocyclyl, etc. (wherein Cyc<sub>2</sub>, Cyc<sub>3</sub> = C3-15 mono-, di-, or tricyclic carbocyclyl or heterocyclyl, etc.; Z = O, S, SO, SO<sub>2</sub>, NH, NHCO, etc.); D = an linking chain consisting of 1-2 or 3-6 of atoms selected from C, N, O, or S, etc.; R<sub>3</sub> = C1-6 alkyl, C3-15 mono-, di-, or tricyclic carbocyclyl, 3- to 15-membered mono-, di-, or tricyclic heterocyclyl, etc.] are prepared These carboxylic acid derivs. include phenylpropanoic acid, phenylpropenoic acid, phenylpropanamide, phenylpropenamide, 3-oxoisindolin-1-ylacetic acid, benzylbenzoic acid, benzylaminoacetic acid, pyrazolylmethylbenzoic acid, benzoylaminoacetic acid, (pyrazolylmethylphenyl)propenoic acid, pyrazolylmethylpropanoic acid, (pyridinyloxyphenyl)propanoic acid, phenoxyacetic acid, phenylbutanoic acid, (pyrazolylmethyl)propanamide, (piperazinylmethylphenyl)propanamide, (morpholinylmethylphenyl)propanamide, (pyridinyloxyphenyl)propanamide, (pyrazolylmethyl)propenamide (oxoimidazolidinylmethylphenyl)propanamide, (oxopyrrolidinylmethylphenyl)propenamide, (thiophenylmethylphenyl)propenamide, (pyrazolylmethylphenylamino)acetamide, (thiazolylaminomethylphenyl)propanamide, thiophenylpropenamide, (pyrazolylmethylphenoxy)acetamide, (phenoxymethyl)benzamide, (pyrazolylmethylphenylethyl)-1,2,4-oxadiazol-5-one, and (pyrazolylmethylphenylindolyl)acetic acid. Because of binding to PEG<sub>2</sub> receptors, in particular, subtype EP<sub>3</sub> and/or subtype EP<sub>4</sub> and having antagonism, the compds. I are useful in preventing and/or treating diseases such as pain, allodynia, hyperalgesia, pruritus (itching), urticaria, atopic dermatitis, contact dermatitis, Urushi (Japanese lacquer tree) dermatitis, allergic conjunctivitis, symptoms during dialysis, asthma, rhinitis, allergic rhinitis, nasal congestion, sneeze, psoriasis, pollakiuria (increased urinary frequency), urination disorder, ejaculation (semination) disorder, fever (pyrexia), systemic inflammation reaction, learning disorder, Alzheimer's disease, neovascularization, cancer formation, cancer proliferation, cancer metastasis to organs, cancer metastasis to bone, hypercalcemia accompanied by cancer metastasis to bone, retinopathy, rubrum, erythema (rash), leucoma, skin moth-patch, heat burn, burn, steroid burn, kidney failure, nephropathy, acute or chronic nephritis, blood electrolyte disorder, imminent abortion, threatened abortion, excessive menstruation, dysmenorrhea, endometriosis, premenstrual syndrome, uterine gland myopathy,

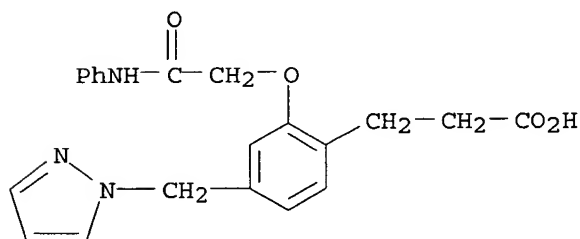
reproduction disorder, and stress. They are also useful in preventing and/or treating anxiety, depression, psychophysiol. disorder, mental retardation, thrombus, embolism, transient ischemic attack, cerebral infarction, atheroma, organ transplant, heart failure, hypertension, myocardial infarction, arteriosclerosis, circulation disorders or ulcers associated therewith, nerve disorders, vascular dementia, edema, diarrhea, constipation, biliary excretion disorder, ulcerative colitis, Crohn's disease, irritable bowel syndrome, reduction of rebound after using steroid drugs, aids for decreasing or removing steroid drugs, bone diseases, systemic granuloma, immune diseases, pyorrhea alveolaris, gingivitis, periodontal disease, nerve cell death, lung disorder, liver disorder, acute hepatitis, myocardial ischemia, Kawasaki disease, multiple organ failure, chronic headache, angiitis, venous failure, varicose vein (varicosis), anal fistula, **diabetes** insipidus, neonatal patent ductus arteriosus, and cholelithiasis. Thus, 4-hydroxymethyl-2-[2-(naphthalen-2-yl)ethoxy]cinnamic acid Et ester was mesylated by methanesulfonyl chloride in the presence of Et<sub>3</sub>N in THF at 0° for 15 min and condensed with pyrazole in the presence of NaH in DMF at 0° to give 2-[2-(naphthalen-2-yl)ethoxy]-4-(1-pyrazolylmethyl)cinnamic acid Et ester. 4-[2-[[2-(Naphthalen-1-yl)propanoyl]amino]-4-methylthiomethylphenyl]butanoic acid inhibited the binding of [3H]PGE<sub>2</sub> to prostaglandin E<sub>2</sub> (PGE<sub>2</sub>) receptor subtype EP<sub>1</sub>, EP<sub>2</sub>, EP<sub>3</sub>, and EP<sub>4</sub> expressed in CHO cells with K<sub>i</sub> of >10, >10, 0.27, and 0.038 μM, resp. A tablet formulation containing (2E)-2-[2-(naphthalen-2-yl)ethoxy]-4-(1-pyrazolylmethyl)cinnamic acid was described.

IT 499145-07-2P 499145-08-3P 499145-09-4P  
499145-20-9P 499145-21-0P 499153-29-6P  
499153-30-9P 499153-40-1P

(preparation of aryl or heterocyclyl-substituted benzoic acid and alkanolic acid derivs. as antagonists of prostaglandin E<sub>2</sub> (PGE<sub>2</sub>) receptors as therapeutic agents)

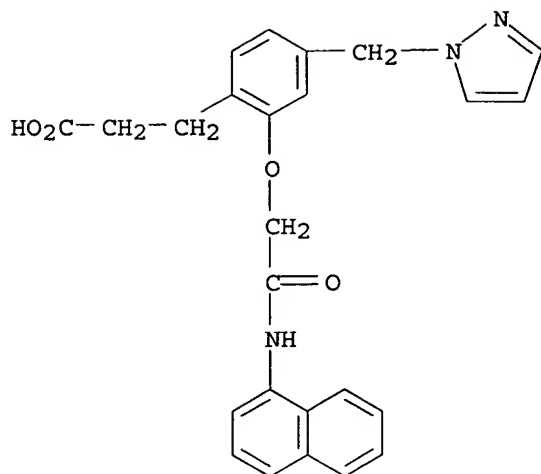
RN 499145-07-2 HCAPLUS

CN Benzenepropanoic acid, 2-[2-oxo-2-(phenylamino)ethoxy]-4-(1H-pyrazol-1-ylmethyl)- (9CI) (CA INDEX NAME)



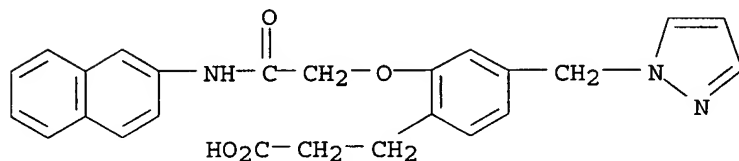
RN 499145-08-3 HCAPLUS

CN Benzenepropanoic acid, 2-[2-(1-naphthalenylamino)-2-oxoethoxy]-4-(1H-pyrazol-1-ylmethyl)- (9CI) (CA INDEX NAME)



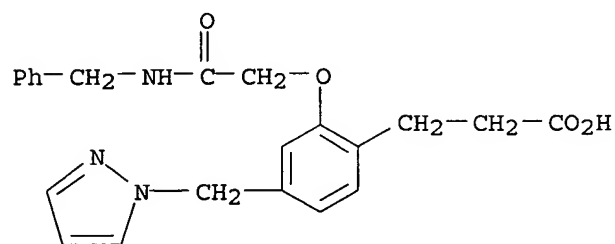
RN 499145-09-4 HCAPLUS

CN Benzenepropanoic acid, 2-[2-(2-naphthalenylamino)-2-oxoethoxy]-4-(1H-pyrazol-1-ylmethyl)- (9CI) (CA INDEX NAME)



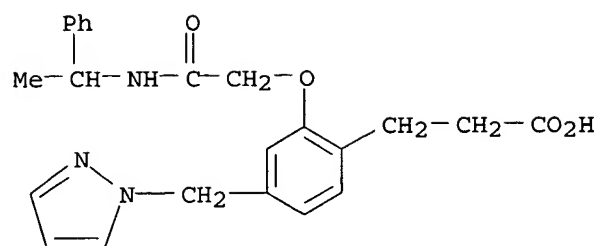
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CN Benzenepropanoic acid, 2-[2-oxo-2-[(phenylmethyl)amino]ethoxy]-4-(1H-pyrazol-1-ylmethyl)- (9CI) (CA INDEX NAME)



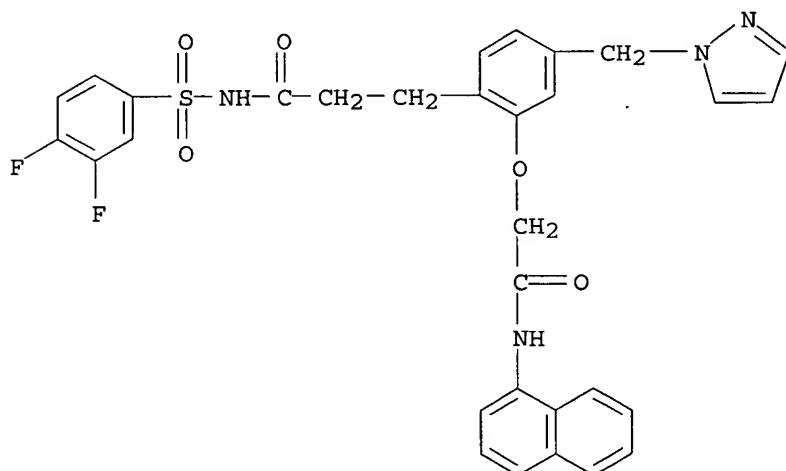
RN 499145-21-0 HCAPLUS

CN Benzenepropanoic acid, 2-[2-oxo-2-[(1-phenylethyl)amino]ethoxy]-4-(1H-pyrazol-1-ylmethyl)- (9CI) (CA INDEX NAME)



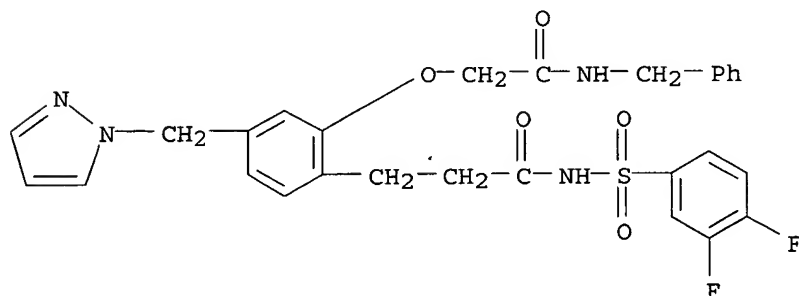
RN 499153-29-6 HCAPLUS

CN Benzenepropanamide, N-[(3,4-difluorophenyl)sulfonyl]-2-[2-(1-naphthalenylamino)-2-oxoethoxy]-4-(1H-pyrazol-1-ylmethyl)- (9CI)  
(CA INDEX NAME)



RN 499153-30-9 HCAPLUS

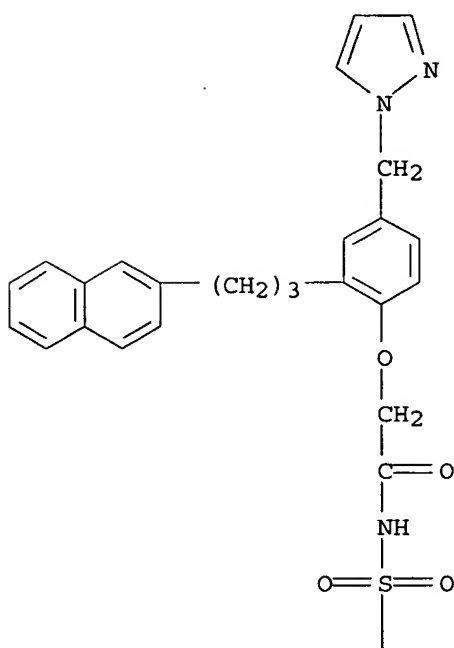
CN Benzenepropanamide, N-[(3,4-difluorophenyl)sulfonyl]-2-[2-oxo-2-[(phenylmethyl)amino]ethoxy]-4-(1H-pyrazol-1-ylmethyl)- (9CI) (CA INDEX NAME)



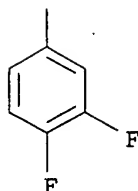
RN 499153-40-1 HCAPLUS

CN Acetamide, N-[(3,4-difluorophenyl)sulfonyl]-2-[2-[3-(2-naphthalenyl)propyl]-4-(1H-pyrazol-1-ylmethyl)phenoxy]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



IC ICM C07C057-40  
 ICS C07C057-44; C07C069-736; C07C229-34; C07C233-47; C07C233-55;  
 C07C233-65; C07C233-81; C07C233-87; C07C235-38; C07C235-42;  
 C07C235-46; C07C235-48; C07C235-54; C07C235-56; C07C237-30;  
 C07C239-18; C07C255-37; C07C255-55; C07C255-57  
 CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))  
 Section cross-reference(s): 25, 27, 63  
 IT Alzheimer's disease  
 Analgesics  
 Anti-Alzheimer's agents  
 Antiarteriosclerotics  
 Antiasthmatics  
 Anticoagulants  
 Antidepressants  
 Antihypertensives  
 Antipyretics  
 Antitumor agents  
 Anxiety

Anxiolytics  
 Arteriosclerosis  
 Asthma  
 Bone, disease  
 Burn  
 Calculi, biliary  
     **Diabetes** insipidus  
 Diarrhea  
 Dysmenorrhea  
 Edema  
 Embolism  
 Fever and Hyperthermia  
 Hypertension  
 Immune disease  
 Immunomodulators  
 Kidney, disease  
 Learning disorders  
 Leucoma  
 Liver, disease  
 Lung, disease  
 Mental retardation  
 Multiple organ failure  
 Nerve, disease  
 Pain  
 Periodontium, disease  
 Pruritus  
 Psoriasis  
 Reproduction disorders  
 Stress, animal  
 Thrombus  
 Transplant and Transplantation  
 Urticaria

(preparation of aryl or heterocycllyl-substituted benzoic acid and  
 alkanolic acid derivs. as antagonists of prostaglandin E2 (PEG2)  
 receptors as therapeutic agents)

IT	499143-62-3P	499143-63-4P	499143-64-5P	499143-65-6P
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(preparation of aryl or heterocyclyl-substituted benzoic acid and  
alkanoic acid derivs. as antagonists of prostaglandin E2 (PEG2)  
receptors as therapeutic agents)

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	499152-51-1P	499152-52-2P	499152-53-3P	499152-54-4P
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499154-23-3P			

(preparation of aryl or heterocyclyl-substituted benzoic acid and alkanolic acid derivs. as antagonists of prostaglandin E2 (PEG2) receptors as therapeutic agents)

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 14 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:942792 HCAPLUS

DOCUMENT NUMBER: 138:24953

TITLE: Preparation of N-sulfonylated phenylalanine dipeptide derivatives as inhibitors of leukocyte adhesion mediated by VLA-4

INVENTOR(S): Thorsett, Eugene D.; Semko, Christopher M.; Sarantakis, Dimitrios; Pleiss, Michael A.; Lombardo, Louis John; Kreft, Anthony; Konradi, Andrei W.; Grant, Francine S.; Dressen, Darren B.; Dappen, Michael S.; Baudy, Reinhardt Bernhard; Ashwell, Susan

PATENT ASSIGNEE(S): Athena Neurosciences, Inc., USA; American Home



SOURCE: Products Corp.  
 U.S., 71 pp.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 6492421	B1	20021210	US 1998-126095	1998 0730

PRIORITY APPLN. INFO.: <--  
 US 1997-104599P P  
 1997  
 0731

OTHER SOURCE(S): MARPAT 138:24953

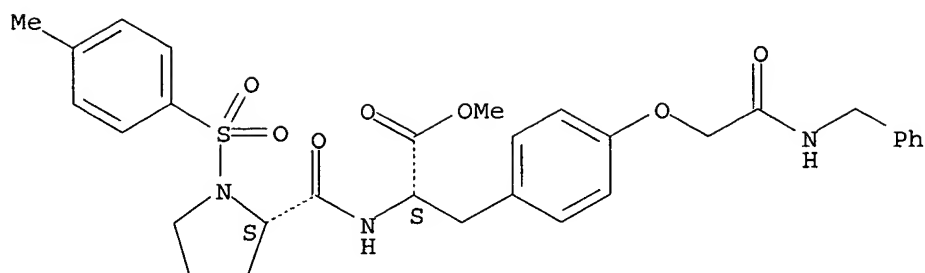
AB Disclosed are title dipeptides R1SO2NR2CHR3-Q-CHR5C02H [R1, R3 = (un)substituted alkyl, aryl, cycloalkyl, heterocyclyl or heteroaryl; R2 = H, (un)substituted cycloalkenyl, or any group given for R1; or R2 may form an (un)substituted heterocyclic ring with R1 or R3; R5 = (CH2)x-Ar-R5'; R5' = alkylcarbonylamino, alkoxyaryl, (hetero)aryl, alkylamino, alkenyl, alkoxyheterocyclyl, etc.; x = 1-4; Ar = (un)substituted (hetero)aryl; Q = C(X)NR7; R7 = H, alkyl; X = O, S (with provisos)] which bind VLA-4 (also referred to as  $\alpha 4\beta 1$  integrin and CD49d/CD29). Certain of these compds. also inhibit leukocyte adhesion and, in particular, leukocyte adhesion mediated by VLA-4. Such compds. are useful in the treatment of inflammatory diseases in a mammalian patient, e.g., human, such as asthma, Alzheimer's disease, atherosclerosis, AIDS dementia, diabetes, inflammatory bowel disease, rheumatoid arthritis, tissue transplantation, tumor metastasis and myocardial ischemia. The compds. can also be administered for the treatment of inflammatory brain diseases such as multiple sclerosis. Thus, condensation of N-tosyl-L-prolyl-4-amino-L-phenylalanine Me ester with N-(tert-butoxycarbonyl)glycine afforded N-tosyl-L-prolyl-4-[(N-tert-butoxycarbonyl)glycyl]amino-L-phenylalanine.

IT 220397-47-7P 220397-52-4P  
 (preparation of N-sulfonylated aminophenylalanine dipeptide derivs. as inhibitors of leukocyte adhesion mediated by VLA-4)

RN 220397-47-7 HCAPLUS

CN L-Tyrosine, 1-[(4-methylphenyl)sulfonyl]-L-prolyl-O-[2-oxo-2-[(phenylmethyl)amino]ethyl]-, methyl ester (9CI) (CA INDEX NAME)

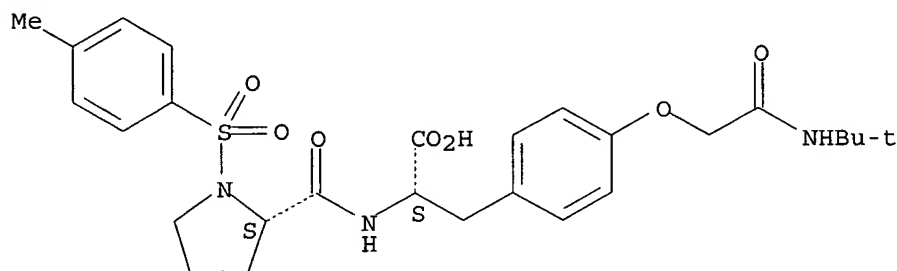
Absolute stereochemistry.



RN 220397-52-4 HCAPLUS

CN L-Tyrosine, 1-[(4-methylphenyl)sulfonyl]-L-prolyl-O-[2-[(1,1-dimethylethyl)amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IC ICM A61K031-19

ICS C07C311-00

INCL 514562000; 514217080; 514227800; 514254010; 514307000; 514363000;  
514365000; 514400000; 514424000; 514542000

CC 34-3 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 1, 63

IT AIDS (disease)

Alzheimer's disease

Anti-inflammatory agents

Antiasthmatics

**Antidiabetic agents**

Antirheumatic agents

Asthma

Atherosclerosis

**Diabetes mellitus**

Encephalitis

Human

Meningitis

Multiple sclerosis

Psoriasis

Rheumatoid arthritis

Transplant and Transplantation

(preparation of N-sulfonylated aminophenylalanine dipeptide derivs.

as inhibitors of leukocyte adhesion mediated by VLA-4)

IT	220396-91-8P	220396-93-0P	220396-94-1P	220396-95-2P
	220396-96-3P	220396-97-4P	220396-98-5P	220396-99-6P
	220397-01-3P	220397-03-5P	220397-04-6P	220397-06-8P
	220397-08-0P	220397-09-1P	220397-10-4P	220397-11-5P
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220398-27-6P 220398-28-7P 220398-29-8P 220398-30-1P  
220398-31-2P

(preparation of N-sulfonylated aminophenylalanine dipeptide derivs.  
as inhibitors of leukocyte adhesion mediated by VLA-4)

REFERENCE COUNT: 84 THERE ARE 84 CITED REFERENCES AVAILABLE  
FOR THIS RECORD. ALL CITATIONS AVAILABLE  
IN THE RE FORMAT

L32 ANSWER 15 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:688154 HCAPLUS

DOCUMENT NUMBER: 137:232648

TITLE: Preparation of pyrrolo[2,1-a]isoindole,  
oxazolo[2,3-a]isoindole, and  
imidazolo[2,3-a]isoindole derivatives as  
remedies for **diabetes** and obesity  
and preventives for chronic **diabetes**  
complications

INVENTOR(S): Iino, Tomoharu; Sato, Yoshiyuki; Nishimura,  
Teruyuki; Banba, Makoto; Eiki, Junichi;  
Nagase, Toshio

PATENT ASSIGNEE(S): Banyu Pharmaceutical Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 124 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

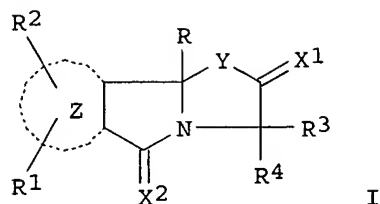
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2002255967	A2	20020911	JP 2001-52973	2001 0227

PRIORITY APPLN. INFO.: JP 2001-52973  
2001  
0227

OTHER SOURCE(S): MARPAT 137:232648  
GI



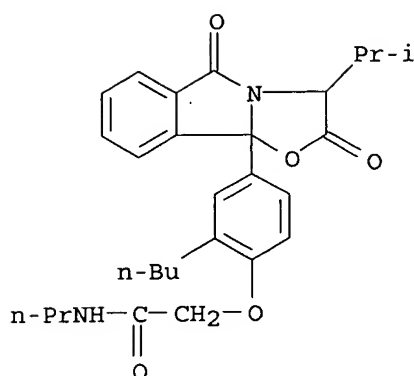
AB Remedies for **diabetes** and obesity or preventives for chronic **diabetes** complications containing the title compds. [I; R = (un)substituted mono to tricyclic C7-15 aromatic group or mono to tricyclic aromatic heterocyclyl containing 1-5 heteroatoms selected from N, O, and S in each ring; R1, R2 = H, N3, NH2, CONH2, carbamoylamino, carbamoyloxy, CO2H, cyano, SO2NH2, SO3H, NO2, halo, HO, CHO, formylamino, cyclic (un)saturated C3-9 aliphatic group, aralkyl, aralkylamino, aralkyloxy, aralkylcarbonyl, aryl, C1-6 alkoxy, linear or branched (un)saturated C1-9 aliphatic group, etc.; R3, R4 = H, N3, amidino, NH2, CONH2, carbamoylamino, carbamoyloxy, CO2H, guanidino, cyano, SO2NH2, SO3H, NO2, halo, HO, CHO, formylamino, cyclic (un)saturated C3-9 aliphatic group, C2-6 alkanoyl, N-C2-6 alkanoylamino, linear or branched (un)saturated C1-9 aliphatic group, etc.; or R3 and R4 together form a linear or branched C1-9 aliphatic group or 5- or 6-membered (un)saturated carbocyclic ring; X1 = O, S, (un)substituted NH; X2 = O, S; Y = O, S, (un)substituted NH or CH2] or pharmaceutically acceptable salts thereof as the active ingredients are claimed. The compds. I exhibits the activity for maintaining the high level of glucagon-like peptide-1 (GLP-1) in blood and improve hyperglycemic state. Thus, to a solution of 750 mg 2-(2-methoxybenzoyl)benzoic acid 550 mg D-valine Me ester hydrochloride in 40 mL CH2Cl2 were added 490 mg 1-hydroxybenzotriazole hydrate, 690 mg 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride, and 1.26 mL Et3N and stirred at room temperature for 3 h, concentrated under reduced pressure, dissolved in 15 MeOH, treated with 8 mL 4 N aqueous NaOH, stirred at room temperature for 12 h, and treated with 40 mL 1 N aqueous HCl and EtOAc. The organic layer was dried, concentrated under reduced pressure to give N-[2-(2-methoxybenzoyl)benzoyl]-D-valine which was stirred with 5 mL CF3CO2H at room temperature for 2 h to give 46% 9b-(2-methoxyphenyl)-3-(1-methylethyl)oxazolo[2,3-a]isoindole-2,5(3H,9bH)-dione. 9B-phenyl-3-(1-methylethyl)oxazolo[2,3-a]isoindole-2,5(3H,9bH)-dione (II) at 30 mg/kg p.o. increased the serum level of GLP-1 from 1.6 pM (control) to 3.8 PM in male Wister rats after 30 min. A capsule formulation containing II was described.

IT 327599-44-0P

(preparation of pyrroloisoindole, oxazoloisoindole, and imidazoloisoindole derivs. for increasing serum GLP-1 activity as remedies for **diabetes** and obesity and preventives for chronic **diabetes** complications)

RN 327599-44-0 HCAPLUS

CN Acetamide, 2-[2-butyl-4-[2,3-dihydro-3-(1-methylethyl)-2,5-dioxoxazolo[2,3-a]isoindol-9b(5H)-yl]phenoxy]-N-propyl- (9CI)  
(CA INDEX NAME)



IC ICM C07D487-04  
 ICS C07D487-04; A61K031-407; A61K031-4188; A61K031-4192;  
 A61K031-437; A61K031-4436; A61K031-4985; A61K031-5025;  
 A61K031-519; A61P003-04; A61P003-10; C07D487-14; C07D498-04;  
 C07D498-14; C07D513-04; C07D513-14

CC 28-9 (Heterocyclic Compounds (More Than One Hetero Atom))  
 Section cross-reference(s): 1, 63

ST pyrroloisoindole oxazoloisoindole imidazoloisoindole prepn  
 treatment **diabetes** obesity; chronic **diabetes**  
 complication treatment oxazoloisoindole prepn

IT **Diabetes mellitus**  
 (chronic complications; preparation of pyrroloisoindole,  
 oxazoloisoindole, and imidazoloisoindole derivs. for increasing  
 serum GLP-1 activity as remedies for **diabetes** and  
 obesity and preventives for chronic **diabetes**  
 complications)

IT **Antidiabetic agents**  
 Antiobesity agents  
**Diabetes mellitus**  
 Obesity  
 (preparation of pyrroloisoindole, oxazoloisoindole, and  
 imidazoloisoindole derivs. for increasing serum GLP-1 activity  
 as remedies for **diabetes** and obesity and preventives  
 for chronic **diabetes** complications)

IT 89750-14-1, Glucagon-like peptide I  
 (preparation of pyrroloisoindole, oxazoloisoindole, and  
 imidazoloisoindole derivs. for increasing serum GLP-1 activity  
 as remedies for **diabetes** and obesity and preventives  
 for chronic **diabetes** complications)

IT 327597-08-0P 327597-09-1P 327597-09-1P 327597-10-4P  
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327599-33-7P	327599-34-8P	327599-35-9P	327599-36-0P
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327599-45-1P	327599-46-2P	327599-47-3P	327599-48-4P

(preparation of pyrroloisindole, oxazoloisindole, and imidazoloisindole derivs. for increasing serum GLP-1 activity as remedies for **diabetes** and obesity and preventives for chronic **diabetes** complications)

IT 327599-49-5P	327599-50-8P	327599-51-9P	327599-52-0P
327599-53-1P	327599-54-2P	327599-55-3P	327599-56-4P
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327599-61-1P	327599-62-2P	327599-63-3P	327599-64-4P
327599-65-5P	327599-66-6P	327599-67-7P	327599-68-8P
327599-69-9P	327599-70-2P	327599-71-3P	327599-72-4P
327599-73-5P	327599-74-6P	327599-75-7P	327599-76-8P
327599-77-9P	327599-78-0P	327599-79-1P	327599-80-4P
327599-81-5P	327599-82-6P	327599-83-7P	327599-85-9P
327599-86-0P	327599-87-1P	327599-88-2P	327599-89-3P
327599-90-6P	327599-91-7P	327599-92-8P	327599-93-9P

327599-94-0P 327599-95-1P 327599-96-2P 327599-97-3P  
 327599-98-4P 327599-99-5P 327600-00-0P 327600-01-1P  
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 327600-28-2P 327600-29-3P 327600-30-6P 327600-31-7P  
 327600-32-8P 327600-33-9P 327600-34-0P 327600-35-1P  
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 327600-40-8P 327600-41-9P 327600-42-0P 327600-43-1P  
 327600-44-2P 327600-45-3P 327600-46-4P 457939-98-9P  
 457939-99-0P 457940-00-0P 457940-01-1P 457940-03-3P  
 457940-04-4P 457940-05-5P 457940-06-6P 457940-07-7P

(preparation of pyrroloisindole, oxazoloisindole, and imidazoloisindole derivs. for increasing serum GLP-1 activity as remedies for **diabetes** and obesity and preventives for chronic **diabetes** complications)

IT 75-16-1, Methylmagnesium bromide. 85-44-9, Phthalic anhydride  
 85-52-9, 2-Benzoylbenzoic acid 578-57-4, 2-Bromoanisole  
 1151-15-1, 2-(4-Methoxybenzoyl)benzoic acid 6638-79-5,  
 N,O-Dimethylhydroxylamine hydrochloride 7146-15-8, D-Valine  
 methyl ester hydrochloride 13139-86-1, 4-Methoxyphenylmagnesium  
 bromide 22838-58-0 70717-76-9

(preparation of pyrroloisindole, oxazoloisindole, and imidazoloisindole derivs. for increasing serum GLP-1 activity as remedies for **diabetes** and obesity and preventives for chronic **diabetes** complications)

IT 1151-04-8P, 2-(2-Methoxybenzoyl)benzoic acid 190260-92-5P  
 327600-47-5P 327600-48-6P 457939-97-8P 457940-02-2P  
 457940-08-8P

(preparation of pyrroloisindole, oxazoloisindole, and imidazoloisindole derivs. for increasing serum GLP-1 activity as remedies for **diabetes** and obesity and preventives for chronic **diabetes** complications)

L32 ANSWER 16 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:658125 HCAPLUS

DOCUMENT NUMBER: 137:201333

TITLE: Preparation of imidazoisindole derivatives, oxazoloisindole derivatives, etc., as remedies for **diabetes** and obesity

INVENTOR(S): Iino, Tomoharu; Bamba, Makoto; Eiki, Junichi; Nagase, Toshio

PATENT ASSIGNEE(S): Banyu Pharmaceutical Co., Ltd., Japan

SOURCE: PCT Int. Appl., 229 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2002066479	A1	20020829	WO 2002-JP1576	2002 0222

<--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA,  
 CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI,  
 GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG,  
 KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK,  
 MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE,  
 SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ,  
 VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT,  
 BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC,  
 NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW,  
 ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

JP 2001-48394

A

2001

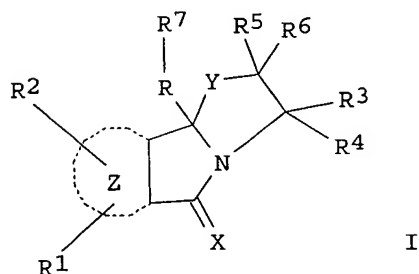
0223

&lt;--

OTHER SOURCE(S):

MARPAT 137:201333

GI



AB The title compds. I [R represents amino, etc.; R1 and R2 are the same or different and each represents hydrogen, etc.; R3, R4, R5 and R6 independently represent each hydrogen, etc.; R7 represents hydrogen, etc.; X represents oxygen, etc.; Y represents oxygen, etc.; and Z represents fused aryl, etc.] are prepared I increase the blood level of GLP-1 (glucagon-like peptide 1) and are useful as remedies for **diabetes**, preventives for chronic complications of **diabetes**, and antiobesity agents. A compound of this invention at 0.3 mg/kg orally caused a significant increase of GLP-1 concentration in blood in rats. Formulations are given.

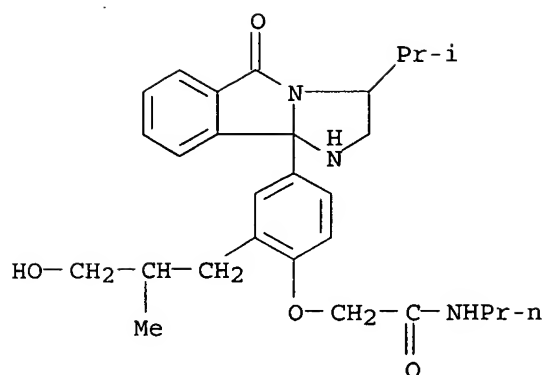
IT 453555-70-9P 453555-72-1P 453555-74-3P

(preparation of imidazoisindole derivs. and oxazoloisindole derivs., as remedies for **diabetes** and obesity)

RN 453555-70-9 HCAPLUS

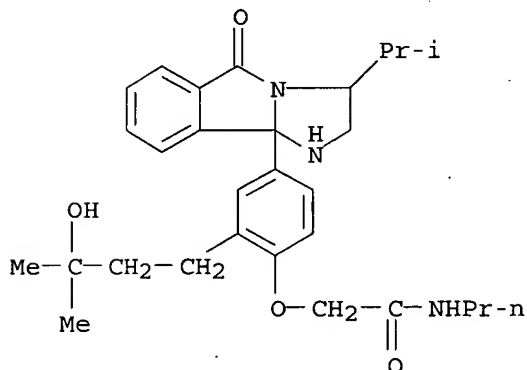
CN Acetamide, 2-[4-[2,3-dihydro-3-(1-methylethyl)-5-oxo-1H-imidazo[2,1-a]isindol-9b(5H)-yl]-2-(3-hydroxy-2-methylpropyl)phenoxy]-N-propyl- (9CI) (CA INDEX NAME)





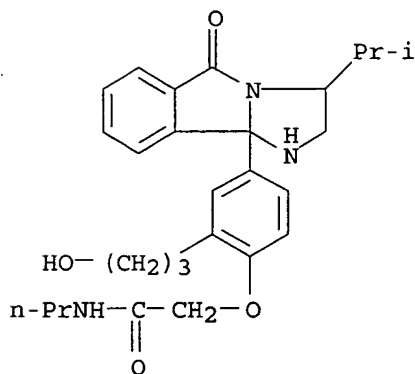
RN 453555-72-1 HCAPLUS

CN Acetamide, 2-[4-[2,3-dihydro-3-(1-methylethyl)-5-oxo-1H-imidazo[2,1-a]isoindol-9b(5H)-yl]-2-(3-hydroxy-3-methylbutyl)phenoxy]-N-propyl- (9CI) (CA INDEX NAME)



RN 453555-74-3 HCAPLUS

CN Acetamide, 2-[4-[2,3-dihydro-3-(1-methylethyl)-5-oxo-1H-imidazo[2,1-a]isoindol-9b(5H)-yl]-2-(3-hydroxypropyl)phenoxy]-N-propyl- (9CI) (CA INDEX NAME)



IC ICM C07D471-04

ICS C07D487-04; C07D498-04; C07D498-14; C07D498-20; C07D513-04;

C07D513-14; C07D513-20; A61K031-424; A61K031-429;  
 A61K031-437; A61K031-4439; A61K031-497; A61K031-4985;  
 A61K031-5025; A61K031-519; A61K031-5377; A61P003-04;  
 A61P003-10; A61P043-00

CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))  
 Section cross-reference(s): 1, 63

ST imidazoisindole oxazoloisindole prepn **diabetes** obesity  
 remedy

IT **Antidiabetic agents**

Antiobesity agents

Obesity

(preparation of imidazoisindole derivs. and oxazoloisindole  
 derivs., as remedies for **diabetes** and obesity)

IT **Diabetes mellitus**

(preparation of imidazoisindole derivs. and oxazoloisindole  
 derivs., as remedies for **diabetes** and obesity, and  
 preventives for complications of **diabetes**.)

IT 89750-14-1, Glucagon-like peptide I

(preparation and effect of imidazoisindole derivs. and  
 oxazoloisindole derivs., as remedies for **diabetes**  
 and obesity)

IT	144692-37-5P	453553-48-5P	453553-50-9P	453553-52-1P
	453553-54-3P	453553-56-5P	453553-58-7P	453553-60-1P
	453553-62-3P	453553-64-5P	453553-66-7P	453553-68-9P
	453553-70-3P	453553-72-5P	453553-74-7P	453553-76-9P
	453553-78-1P	453553-80-5P	453553-82-7P	453553-84-9P
	453553-86-1P	453553-88-3P	453553-90-7P	453553-92-9P
	453553-94-1P	453553-96-3P	453553-98-5P	453554-00-2P
	453554-02-4P	453554-04-6P	453554-06-8P	453554-08-0P
	453554-10-4P	453554-12-6P	453554-14-8P	453554-16-0P
	453554-18-2P	453554-20-6P	453554-22-8P	453554-24-0P
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	453554-34-2P	453554-36-4P	453554-38-6P	453554-40-0P
	453554-42-2P	453554-44-4P	453554-46-6P	453554-48-8P
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	453554-66-0P	453554-68-2P	453554-70-6P	453554-72-8P
	453554-74-0P	453554-76-2P	453554-78-4P	453554-80-8P
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	453555-76-5P	453555-79-8P	453555-81-2P	453555-83-4P
	453555-85-6P	453555-87-8P	453555-89-0P	453555-91-4P
	453555-93-6P			

(preparation of imidazoisindole derivs. and oxazoloisindole  
 derivs., as remedies for **diabetes** and obesity)

IT 67-56-1, Methanol, reactions 85-44-9, Phthalic anhydride  
 5395-67-5, 2-Bromo-N-propylacetamide 7439-95-4, Magnesium,  
 reactions 14804-31-0, 4-Bromo-2-methylanisole 453556-02-0  
 453556-04-2 453556-06-4

(preparation of imidazoisindole derivs. and oxazoloisindole

derivs., as remedies for **diabetes** and obesity)

IT 51671-71-7P 93012-28-3P 97356-10-0P 453555-98-1P  
453556-00-8P

(preparation of imidazoisindole derivs. and oxazoloisindole  
derivs., as remedies for **diabetes** and obesity)

REFERENCE COUNT: 61 THERE ARE 61 CITED REFERENCES AVAILABLE  
FOR THIS RECORD. ALL CITATIONS AVAILABLE  
IN THE RE FORMAT

L32 ANSWER 17 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:516372 HCAPLUS

DOCUMENT NUMBER: 137:78955

TITLE: Preparation of benzimidazole- $\alpha$ -  
substituted carboxylic acid derivatives for  
prevention and/or treatment of diseases such  
as **diabetes**

INVENTOR(S): Fujita, Takashi; Wada, Kunio; Oguchi, Minoru;  
Honma, Hidehito; Fujiwara, Toshihiko;  
Iwabuchi, Haruo

PATENT ASSIGNEE(S): Sankyo Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 93 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

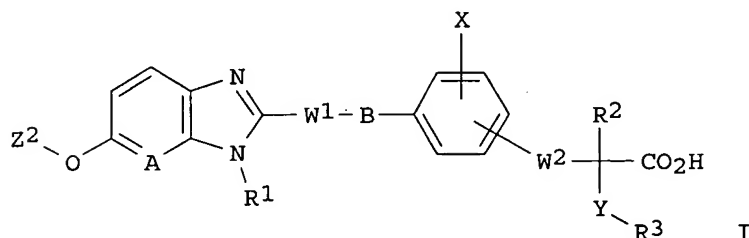
LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. -----	KIND ----	DATE -----	APPLICATION NO. -----	DATE
JP 2002193948	A2	20020710	JP 2001-308762	2001 1004
			<--	
PRIORITY APPLN. INFO.:			JP 2000-307158	A 2000 1006
			<--	

OTHER SOURCE(S): MARPAT 137:78955  
GI



AB Disclosed are insulin-resistance improving agents, blood  
sugar-lowering agents, immune regulating agents, aldose  
reductase-inhibitors, 5-lipoxygenase-inhibitors, lipid peroxide  
formation-suppressing agents, **peroxisome**  
proliferator-activated receptor (PPAR)-activating agents  
leukotriene antagonists, fat cell-formation promoters, and calcium

antagonists containing the title compds. [I; R1, R2, R3 = H, C1-6 alkyl, (un)substituted C6-10 aryl, (un)substituted C7-16 , C1-6 alkylsulfonyl, C1-6 haloalkylsulfonyl, (un)substituted C6-10 arylsulfonyl, C7-16 aralkylsulfonyl; A = N, CH; B = O, S; W1 = C1-6 alkylene; W2 = single bond, C1-8 alkylene; X = H, C1-6 alkyl, C1-6 haloalkyl, C1-6 alkoxy, halo, HO, cyano, NO2, C3-10 cycloalkyl, (un)substituted C6-10 aryl, (un)substituted C7-16 aralkyl, C1-7 aliphatic acyl, C4-11 cycloalkylcarbonyl, (un)substituted C7-11 arylcarbonyl, C8-17 aralkylcarbonyl, (un)substituted monocyclic heterocyclylcarbonyl, CONH2, (un)substituted C7-11 arylaminocarbonyl, (un)substituted NH2; Y = O, S(O)p (p = 0-2); Z2 = (un)substituted saturated heterocyclyl or C6-10 aryl] or pharmacol. acceptable salts as the active ingredients. They are useful for the prevention and/or treatment of **diabetes**, impaired glucose tolerance, neurosis, cataract, coronary artery disease, and gestational **diabetes**. Thus, a solution of 3-[4-[[[4-[4-(adamantan-1-yl)phenoxy]-2-(N-tert-butoxycarbonyl-N-methylamino)phenyl]amino]carbonyl]methoxy]phenyl]-2-(4-fluorobenzyloxy)propionic acid Me ester in 4 N HCl/dioxane was stirred at room temperature for 1 h to give 3-[4-[6-[4-(adamantan-1-yl)phenoxy]-1-methyl-1H-benzimidazol-2-yl]methoxy]phenyl]-2-(4-fluorobenzyloxy)propanoic acid Me ester which was stirred with a mixture of 2 n aqueous NaOH and methanol at room temperature for 2 h, treated with THF, stirred for 4 h, poured into water, and neutralized with HCl and aqueous NaHCO3 to give 3-[4-[6-[4-(adamantan-1-yl)phenoxy]-1-methyl-1H-benzimidazol-2-yl]methoxy]phenyl]-2-(4-fluorobenzyloxy)propanoic acid (II). When a feed containing 0.01% II was fed to **diabetic** KK mice for 3 days, blood sugar level was lowered by 58.5%. A capsule, a tablet, and a granule formulation containing II were prepared

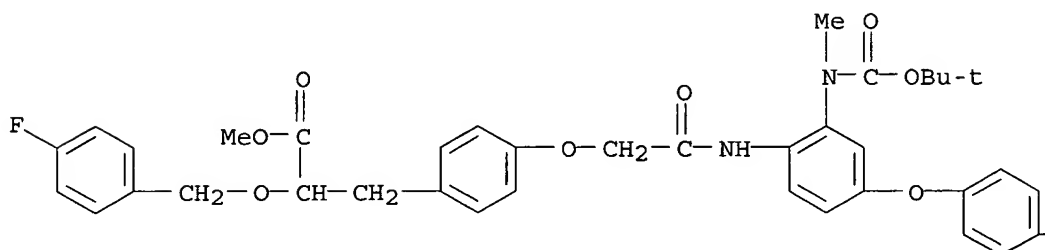
IT 299175-84-1P 299175-86-3P 299175-96-5P  
299176-05-9P

(preparation of benzimidazole- $\alpha$ -substituted carboxylic acid derivs. for prevention and/or treatment of diseases such as **diabetes** and impaired glucose tolerance)

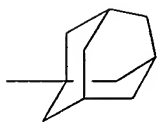
RN 299175-84-1 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[2-[[[(1,1-dimethylethoxy)carbonyl]methylamino]-4-(4-*tricyclo*[3.3.1.1<sup>3,7</sup>]dec-1-ylphenoxy)phenyl]amino]-2-oxoethoxy]- $\alpha$ -(4-fluorophenyl)methoxy]-, methyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



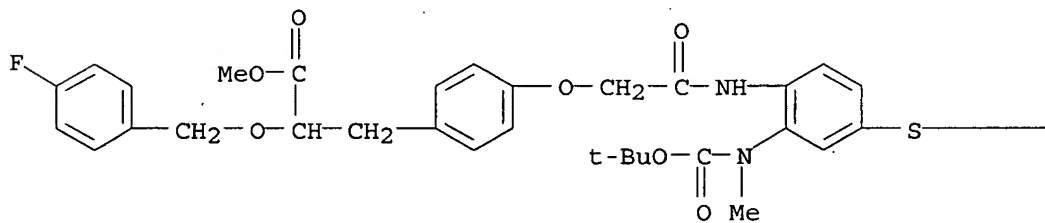
PAGE 1-B



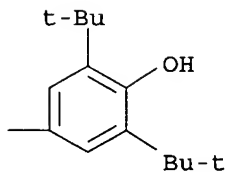
RN 299175-86-3 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[4-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-2-[[[(1,1-dimethylethoxy)carbonyl]methylamino]phenyl]amino]-2-oxoethoxy]- $\alpha$ -(4-fluorophenyl)methoxy]-, methyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

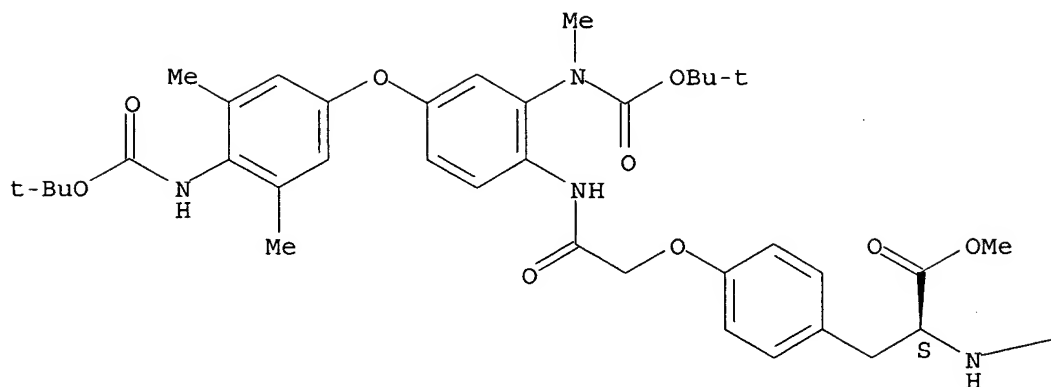


RN 299175-96-5 HCAPLUS

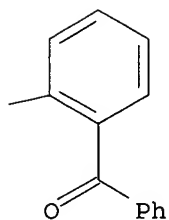
CN L-Tyrosine, N-(2-benzoylphenyl)-O-[2-[[4-[4-[[[(1,1-dimethylethoxy)carbonyl]amino]-3,5-dimethylphenoxy]-2-[[[(1,1-dimethylethoxy)carbonyl]methylamino]phenyl]amino]-2-oxoethyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

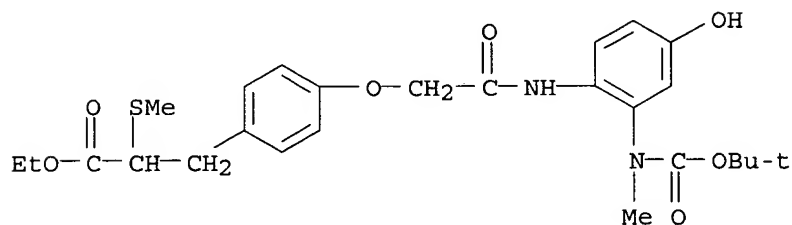


PAGE 1-B



RN 299176-05-9 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[2-[[[(1,1-dimethylethoxy)carbonyl]methylamino]-4-hydroxyphenyl]amino]-2-oxoethoxy]- $\alpha$ -(methylthio)-, ethyl ester (9CI) (CA INDEX NAME)



IC ICM C07D235-12

ICS A61K031-4184; A61K031-7056; A61P001-00; A61P001-04;

- A61P001-16; A61P003-00; A61P003-04; A61P003-06; A61P003-10;  
A61P005-24; A61P009-00; A61P009-10; A61P009-12; A61P011-06;  
A61P013-12; A61P015-00; A61P017-00; A61P017-06; A61P019-02
- CC 28-9 (Heterocyclic Compounds (More Than One Hetero Atom))  
Section cross-reference(s): 1, 7, 63
- ST benzimidazole substituted carboxylic acid prepn prevention  
treatment **diabetes**; impaired glucose tolerance  
prevention treatment phenylpropanoic acid prepn; neurosis cataract  
phenylpropanoic acid prepn; coronary artery disease  
phenylpropanoic acid prepn; gestational **diabetes**  
phenylpropanoic acid prepn; benzimidazolylmethoxyphenylfluorobenzy  
loxypropanoic acid prepn calcium antagonist;  
phenylfluorobenzyloxypropanoic acid benzimidazolylmethoxy prepn;  
insulin resistance improver phenylpropanoic acid prepn; blood  
sugar lowering agent phenylpropanoic acid prepn; immune regulating  
agent phenylpropanoic acid prepn; aldose reductase inhibitor  
phenylpropanoic acid prepn; lipoxxygenase inhibitor phenylpropanoic  
acid prepn; lipid peroxide formation suppressant phenylpropanoic  
acid prepn; **peroxisome** proliferator activated receptor  
activator phenylpropanoic acid prepn; leukotriene antagonist  
phenylpropanoic acid prepn; fat cell formation promoter  
phenylpropanoic acid prepn; calcium antagonist phenylpropanoic  
acid prepn
- IT **Peroxisome** proliferator-activated receptors  
(activators; preparation of benzimidazole- $\alpha$ -substituted  
carboxylic acid derivs. for prevention and/or treatment of  
diseases such as **diabetes** and impaired glucose  
tolerance)
- IT Adipose tissue  
(adipocyte, formation promoters; preparation of benzimidazole-  
 $\alpha$ -substituted carboxylic acid derivs. for prevention  
and/or treatment of diseases such as **diabetes** and  
impaired glucose tolerance)
- IT Artery, disease  
(coronary; preparation of benzimidazole- $\alpha$ -substituted  
carboxylic acid derivs. for prevention and/or treatment of  
diseases such as **diabetes** and impaired glucose  
tolerance)
- IT Pregnancy disorders  
(gestational **diabetes**; preparation of benzimidazole-  
 $\alpha$ -substituted carboxylic acid derivs. for prevention  
and/or treatment of diseases such as **diabetes** and  
impaired glucose tolerance)
- IT Peroxides, biological studies  
(lipid, formation inhibitors; preparation of benzimidazole- $\alpha$ -  
substituted carboxylic acid derivs. for prevention and/or  
treatment of diseases such as **diabetes** and impaired  
glucose tolerance)
- IT Mental and behavioral disorders  
(neurosis; preparation of benzimidazole- $\alpha$ -substituted  
carboxylic acid derivs. for prevention and/or treatment of  
diseases such as **diabetes** and impaired glucose  
tolerance)
- IT Lipids, biological studies  
(peroxides, formation inhibitors; preparation of  
benzimidazole- $\alpha$ -substituted carboxylic acid derivs. for  
prevention and/or treatment of diseases such as  
**diabetes** and impaired glucose tolerance)
- IT Calcium channel blockers  
Cataract

**Diabetes mellitus**

## Immunomodulators

## Leukotriene antagonists

(preparation of benzimidazole- $\alpha$ -substituted carboxylic acid derivs. for prevention and/or treatment of diseases such as **diabetes** and impaired glucose tolerance)

## IT Carboxylic acids, preparation

(preparation of benzimidazole- $\alpha$ -substituted carboxylic acid derivs. for prevention and/or treatment of diseases such as **diabetes** and impaired glucose tolerance)

## IT 1548-13-6, 4-(Trifluoromethyl)phenyl isocyanate

(N-carbamoylation; preparation of benzimidazole- $\alpha$ -substituted carboxylic acid derivs. for prevention and/or treatment of diseases such as **diabetes** and impaired glucose tolerance)

## IT 299176-22-0

(S-acetylation; preparation of benzimidazole- $\alpha$ -substituted carboxylic acid derivs. for prevention and/or treatment of diseases such as **diabetes** and impaired glucose tolerance)

## IT 440355-17-9

(S-methylation; preparation of benzimidazole- $\alpha$ -substituted carboxylic acid derivs. for prevention and/or treatment of diseases such as **diabetes** and impaired glucose tolerance)

## IT 306-23-0, 3-(4-Hydroxyphenyl)lactic acid

(acetonation of hydroxyphenyllactic acid; preparation of benzimidazole- $\alpha$ -substituted carboxylic acid derivs. for prevention and/or treatment of diseases such as **diabetes** and impaired glucose tolerance)

## IT 299176-28-6

(amidation with ammonia; preparation of benzimidazole- $\alpha$ -substituted carboxylic acid derivs. for prevention and/or treatment of diseases such as **diabetes** and impaired glucose tolerance)

## IT 179087-93-5

(amidation with aniline derivative; preparation of benzimidazole- $\alpha$ -substituted carboxylic acid derivs. for prevention and/or treatment of diseases such as **diabetes** and impaired glucose tolerance)

## IT 314271-24-4

(amidation with phenoxyacetic acid derivative; preparation of benzimidazole- $\alpha$ -substituted carboxylic acid derivs. for prevention and/or treatment of diseases such as **diabetes** and impaired glucose tolerance)

## IT 459-46-1, 4-Fluorobenzyl bromide

(benzylation of phenyllactic acid derivative; preparation of benzimidazole- $\alpha$ -substituted carboxylic acid derivs. for prevention and/or treatment of diseases such as **diabetes** and impaired glucose tolerance)

## IT 299176-17-3

(etherification with adamantylphenol; preparation of benzimidazole- $\alpha$ -substituted carboxylic acid derivs. for prevention and/or treatment of diseases such as **diabetes** and impaired glucose tolerance)

## IT 3096-70-6, 4-Amino-3,5-dimethylphenol

(etherification with chloronitrobenzene derivative; preparation of benzimidazole- $\alpha$ -substituted carboxylic acid derivs. for prevention and/or treatment of diseases such as **diabetes** and impaired glucose tolerance)



- IT 157439-51-5  
(etherification with methoxymethyl chloride; preparation of benzimidazole- $\alpha$ -substituted carboxylic acid derivs. for prevention and/or treatment of diseases such as **diabetes** and impaired glucose tolerance)
- IT 5437-45-6, Benzyl bromoacetate  
(etherification with phenol derivative; preparation of benzimidazole- $\alpha$ -substituted carboxylic acid derivs. for prevention and/or treatment of diseases such as **diabetes** and impaired glucose tolerance)
- IT 51095-47-7  
(etherification with tert-Bu bromoacetate or acetonation with acetone; preparation of benzimidazole- $\alpha$ -substituted carboxylic acid derivs. for prevention and/or treatment of diseases such as **diabetes** and impaired glucose tolerance)
- IT 7355-18-2  
(glycosidation with hydroxybenzimidazole derivative; preparation of benzimidazole- $\alpha$ -substituted carboxylic acid derivs. for prevention and/or treatment of diseases such as **diabetes** and impaired glucose tolerance)
- IT 50-99-7, D-Glucose, biological studies  
(impaired glucose tolerance; preparation of benzimidazole- $\alpha$ -substituted carboxylic acid derivs. for prevention and/or treatment of diseases such as **diabetes** and impaired glucose tolerance)
- IT 9028-31-3, Aldose reductase 80619-02-9, 5-Lipoxygenase  
(inhibitors; preparation of benzimidazole- $\alpha$ -substituted carboxylic acid derivs. for prevention and/or treatment of diseases such as **diabetes** and impaired glucose tolerance)
- IT 299175-55-6P 299175-56-7P 299175-57-8P 299175-68-1P  
299175-74-9P 299175-75-0P 299175-77-2P 299175-78-3P  
299176-10-6P 440355-00-0P 440355-03-3P 440355-05-5P  
440355-06-6P 440355-10-2P 440355-12-4P  
(preparation of benzimidazole- $\alpha$ -substituted carboxylic acid derivs. for prevention and/or treatment of diseases such as **diabetes** and impaired glucose tolerance)
- IT 299175-39-6P 299175-40-9P 299175-41-0P 299175-44-3P  
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440355-18-0P 440355-21-5P 440355-22-6P 440355-23-7P  
440355-24-8P 440355-25-9P  
(preparation of benzimidazole- $\alpha$ -substituted carboxylic acid derivs. for prevention and/or treatment of diseases such as **diabetes** and impaired glucose tolerance)
- IT 5292-43-3, tert-Butyl bromoacetate 29799-07-3,  
4-(1-Adamantyl)phenol  
(preparation of benzimidazole- $\alpha$ -substituted carboxylic acid derivs. for prevention and/or treatment of diseases such as **diabetes** and impaired glucose tolerance)
- IT 196810-09-0P 197299-03-9P 223133-10-6P 223133-16-2P  
223133-17-3P 223133-29-7P 223133-30-0P 223133-31-1P  
223133-34-4P 223133-45-7P 223133-70-8P 299175-79-4P  
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299176-06-0P 299176-07-1P 321595-74-8P 332944-40-8P  
440355-16-8P

(preparation of benzimidazole- $\alpha$ -substituted carboxylic acid derivs. for prevention and/or treatment of diseases such as **diabetes** and impaired glucose tolerance)

IT 299176-23-1P

(rat's metabolite; preparation of benzimidazole- $\alpha$ -substituted carboxylic acid derivs. for prevention and/or treatment of diseases such as **diabetes** and impaired glucose tolerance)

IT 3580-38-9, 2-Benzoylcyclohexanone

(reductive amination and aromatization; preparation of benzimidazole- $\alpha$ -substituted carboxylic acid derivs. for prevention and/or treatment of diseases such as **diabetes** and impaired glucose tolerance)

IT 3417-91-2, L-Tyrosine methyl ester hydrochloride

(reductive amination of benzoylcyclohexanone; preparation of benzimidazole- $\alpha$ -substituted carboxylic acid derivs. for prevention and/or treatment of diseases such as **diabetes** and impaired glucose tolerance)

IT 9004-10-8, Insulin, biological studies

(resistance improver; preparation of benzimidazole- $\alpha$ -substituted carboxylic acid derivs. for prevention and/or treatment of diseases such as **diabetes** and impaired glucose tolerance)

IT 299176-11-7

(ring-cleavage and esterification with ethanol; preparation of benzimidazole- $\alpha$ -substituted carboxylic acid derivs. for prevention and/or treatment of diseases such as **diabetes** and impaired glucose tolerance)

IT 150556-70-0

(ring-opening hydrolysis; preparation of benzimidazole- $\alpha$ -substituted carboxylic acid derivs. for prevention and/or treatment of diseases such as **diabetes** and impaired glucose tolerance)

IT 950-59-4

(thioetherification with chloronitroaniline derivative; preparation of benzimidazole- $\alpha$ -substituted carboxylic acid derivs. for prevention and/or treatment of diseases such as **diabetes** and impaired glucose tolerance)

L32 ANSWER 18 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:484863 HCAPLUS

DOCUMENT NUMBER: 137:47448

TITLE: Preparation of substituted phenylalaninol derivatives as protein tyrosine phosphatase inhibitors

INVENTOR(S): Larsen, Scott D.; May, Paul D.; Bleasdale, John E.; Liljebris, Charlotta; Schostarez, Heinrich Josef; Barf, Tjeerd; Nilsson, Marianne

PATENT ASSIGNEE(S): USA

SOURCE: U.S., 144 pp., Cont.-in-part of U.S. Ser. No. 138,642.

CODEN: USXXAM

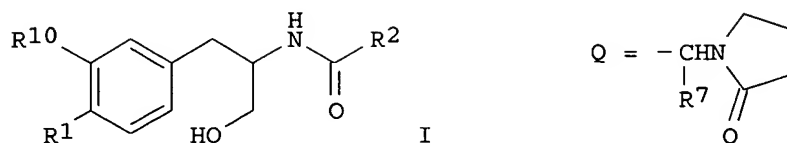
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6410585	B1	20020625	US 1999-265410	1999 0310
US 6353023	B1	20020305	US 1998-138642	1998 0824
CA 2366308	AA	20000914	CA 2000-2366308	2000 0309
WO 2000053583	A1	20000914	WO 2000-US6022	2000 0309
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1161421	A1	20011212	EP 2000-917793	2000 0309
JP 2002539115	T2	20021119	JP 2000-604023	2000 0309
AU 769511	B2	20040129	AU 2000-38711	2000 0309
PRIORITY APPLN. INFO.: US 1997-57730P P 1997 0828 US 1998-138642 A2 1998 0824 US 1999-265410 A 1999 0310 WO 2000-US6022 W				

2000  
0309OTHER SOURCE(S): MARPAT 137:47448  
GI

AB The invention comprises phenylalaninol derivs., e.g., I [R1 = OSO<sub>3</sub>H, OCH(CO<sub>2</sub>R<sub>5</sub>)<sub>2</sub>, OCH<sub>2</sub>CO<sub>2</sub>R<sub>5</sub>, OCH(CO<sub>2</sub>R<sub>5</sub>)CH<sub>2</sub>CO<sub>2</sub>R<sub>5</sub>, OC(CO<sub>2</sub>R<sub>5</sub>):CHCO<sub>2</sub>R<sub>5</sub>, CH<sub>2</sub>CH(CO<sub>2</sub>R<sub>5</sub>)<sub>2</sub>, CH:C(CO<sub>2</sub>R<sub>5</sub>)<sub>2</sub>, OCH<sub>2</sub>CONHOH, N(CH<sub>2</sub>CO<sub>2</sub>R<sub>5</sub>)<sub>2</sub>, OCHFCO<sub>2</sub>R<sub>5</sub> (R<sub>5</sub> = H, alkyl, alkylphenyl); R<sub>2</sub> = CHR<sub>7</sub>NHXR<sub>6</sub>, group Q (R<sub>6</sub> = alkyl, alkyl-CONH<sub>2</sub>, alkyl-NHCO<sub>2</sub>R<sub>5</sub>, etc.; R<sub>7</sub> = H, any group given for R<sub>6</sub>); R<sub>10</sub> = H, CO<sub>2</sub>R<sub>5</sub>, CONHOH, 5-tetrazolyl, F, OCH<sub>2</sub>CO<sub>2</sub>R<sub>5</sub>], or their pharmaceutically acceptable salts, as small mol. weight, non-peptidic inhibitors of protein tyrosine phosphatase 1 (PTP1) which are useful for the treatment and/or prevention of non-insulin dependent **diabetes** mellitus. Thus, 5-[(2S)-2-[[[(2S)-2-[(tert-butoxycarbonyl)amino]-3-phenylpropanoyl]amino]-3-hydroxypropyl]-2-(carboxymethoxy)benzoic acid (claimed compound) was prepared and showed 80% inhibition of protein tyrosine phosphatase 1B at a concentration of 10 μM.

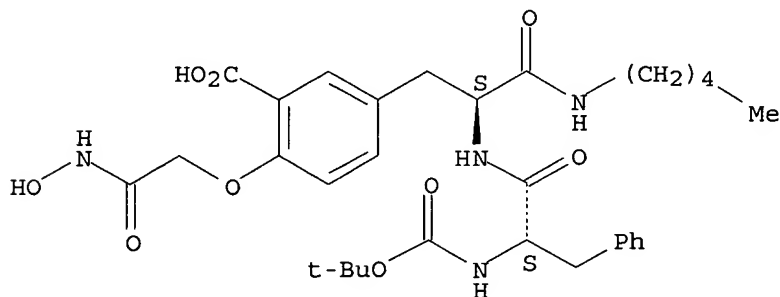
IT 221076-84-2P

(preparation of substituted phenylalanine derivs. as protein tyrosine phosphatase inhibitors)

RN 221076-84-2 HCAPLUS

CN L-Tyrosinamide, N-[(1,1-dimethylethoxy)carbonyl]-L-phenylalanyl-3-carboxy-O-[2-(hydroxyamino)-2-oxoethyl]-N-pentyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



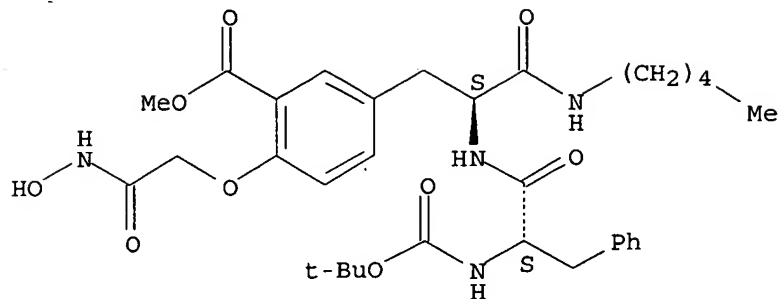
IT 221077-60-7P

(preparation of substituted phenylalanine derivs. as protein tyrosine phosphatase inhibitors)

RN 221077-60-7 HCAPLUS

CN L-Tyrosinamide, N-[(1,1-dimethylethoxy)carbonyl]-L-phenylalanyl-O-[2-(hydroxyamino)-2-oxoethyl]-3-(methoxycarbonyl)-N-pentyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IC ICM C07C235-00  
ICS C07C237-22; A61K031-165  
INCL 514424000  
CC 34-3 (Amino Acids, Peptides, and Proteins)  
Section cross-reference(s): 1, 7, 63  
ST phenylalaninol deriv prepn protein tyrosine phosphatase inhibitor;  
noninsulin dependent **diabetes** mellitus treatment  
phenylalaninol deriv prepn  
IT **Diabetes** mellitus  
(non-insulin-dependent; preparation of substituted phenylalanine  
derivs. as protein tyrosine phosphatase inhibitors)  
IT 221075-08-7P 221075-11-2P 221075-12-3P 221075-13-4P  
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292835-80-4P	292835-81-5P	292835-82-6P	292835-83-7P

(preparation of substituted phenylalanine derivs. as protein tyrosine phosphatase inhibitors)

IT	2222-15-3P	4521-18-0P	4619-18-5P	38336-04-8P	40829-20-7P
	40904-59-4P	63998-62-9P	71400-63-0P	72457-26-2P	
	83708-38-7P	83708-39-8P	108376-28-9P	134081-15-5P	
	141360-76-1P	159560-93-7P	221076-98-8P	221077-00-5P	
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	438588-24-0P				

(preparation of substituted phenylalanine derivs. as protein tyrosine phosphatase inhibitors)

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 19 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:368462 HCAPLUS

DOCUMENT NUMBER: 136:386118

TITLE: Preparation of (phenylalkyl)-1H-[1,2,4]triazolones as PPAR $\alpha$  agonists for treatment of cardiovascular disease associated

INVENTOR(S): with Syndrome X and related conditions  
 Mantlo, Nathan Bryan; Collado Cano, Ivan;  
 Dominianni, Samuel James; Etgen, Garret Jay,  
 Jr.; Garcia-Paredes, Cristina; Johnston,  
 Richard Duane; Letourneau, Michael Edward;  
 Martinelli, Michael John; Mayhugh, Daniel Ray;  
 Saeed, Ashraf; Thompson, Richard Craig; Wang,  
 Xiadong; Coffey, David Scott; Schmid,  
 Christopher Randall; Vicenzi, Jeffrey Thomas;  
 Xu, Yanping

PATENT ASSIGNEE(S): Eli Lilly and Company, USA

SOURCE: PCT Int. Appl., 388 pp.  
 CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002038553	A2	20020516	WO 2001-US42928	2001 1109
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WO 2002038553	A3	20030501		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2421154	AA	20020516	CA 2001-2421154	2001 1109
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AU 2002028592	A5	20020521	AU 2002-28592	2001 1109
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EP 1335908	A2	20030820	EP 2001-989704	2001 1109
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PRIORITY APPLN. INFO.:

US 2000-247317P

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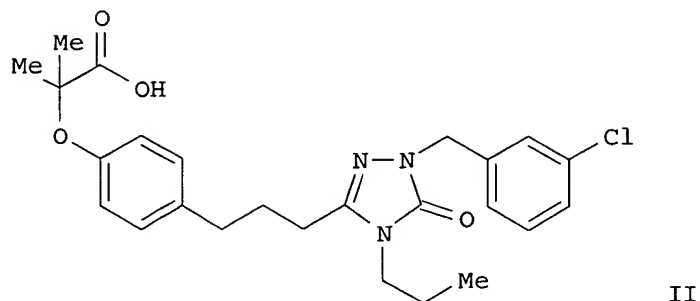
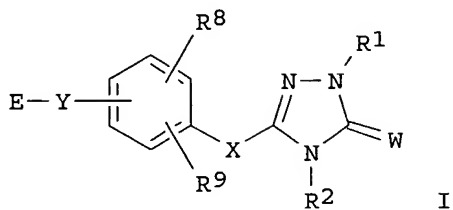
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WO 2001-US42928

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MARPAT 136:386118





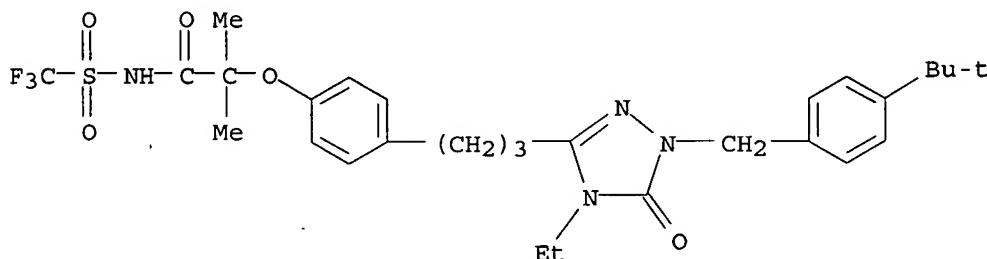
AB Title compds. I [wherein R1 = H or (un)substituted alkyl, (hetero)arylalkyl, cycloalkylarylalkyl, CH<sub>2</sub>COR17R18; R17 = O or NH; R18 = (un)substituted benzyl; W = O or S; R2 = H or (un)substituted (cyclo)alkyl, allyl, (hetero)arylalkyl, sulfonamido, amido, or OR10; R10 = H or alkyl; X = (un)substituted alkylene linker wherein 1 C may be replaced with O, NH, or S; Y = C, O, S, NH, or a single bond; E = H, CR<sub>3</sub>R<sub>4</sub>A; A, (un)substituted (CH<sub>2</sub>)<sub>n</sub>CO<sub>2</sub>C19, (aryl)alkyl, allyl, thioalkyl, thioaryl, alkoxyaryl, alkoxyalkyl, aminoaryl, or aminoalkyl; n = 0-3; A = carboxy, alkynitrile, carboxamide, or (un)substituted sulfonamide, acylsulfonamide, or tetrazole; R3 = H, alkyl, or alkoxy; R4 = H, halo, or (un)substituted (cyclo)alkyl, alkoxy, arylalkyl, or Ph; or CR<sub>3</sub>R<sub>4</sub> = cycloalkyl; R19 = H or (un)substituted arylmethyl or alkyl; R8 = independently H, alkyl, alkenyl, or halo; R9 = independently H, alkenyl, halo, allyl, OR10, or (un)substituted alkyl or (hetero)aryl; R10 = independently H or alkyl] were prepared as peroxisome proliferator activated receptor alpha (PPAR $\alpha$ ) agonists. For example, condensation of 3-chlorobenzaldehyde with 4-(4-hydroxyphenyl)butyrylhydrazide (p-TsOH, i-PrOH), followed by reduction (NaBH<sub>3</sub>CN, THF, AcOH, i-PrOH), treatment with n-PrNCO (THF), and cyclization (KOH, MeOH), afforded 2-(3-chlorobenzyl)-5-[3-(4-hydroxyphenyl)propyl]-4-propyl-3H-triazolin-3-one. Addition of tert-Bu 2-bromoisobutyrate (K<sub>2</sub>CO<sub>3</sub>, DMF) and deesterification (TFA, CH<sub>2</sub>Cl<sub>2</sub>) gave II. I bound to PPAR $\alpha$  receptors with IC<sub>50</sub> values of  $\leq$  100 nM and demonstrated PPAR $\alpha$  cotransfection efficacy in CV-1 cells of  $\geq$  50%. Significant reduction in RQ in female Ay mice [0.864  $\pm$  0.013 (control) vs. 0.803  $\pm$  0.007 (treated); p < 0.001] was observed at doses of 50 mg/kg of I. Addnl., treated animals displayed significantly higher rates of energy expenditure than control animals (17.40  $\pm$  0.49 vs. 13.62  $\pm$  0.26 kcal/kg/h, resp.). Thus, I are useful for the prevention and/or treatment of cardiovascular disease associated with Syndrome X, hyperinsulemia, hypertension, elevated body weight, elevate triglycerides, and elevated LDL.

IT 425671-55-2P 425671-56-3P 425671-57-4P  
425671-58-5P 425671-59-6P 425671-60-9P  
425671-61-0P 425671-62-1P 425671-63-2P  
425671-77-8P 425671-78-9P 425671-79-0P

(cardiovascular agent; preparation of (phenylalkyl)triazolones as PPAR $\alpha$  agonists for treatment of cardiovascular disease associated with Syndrome X and related conditions)

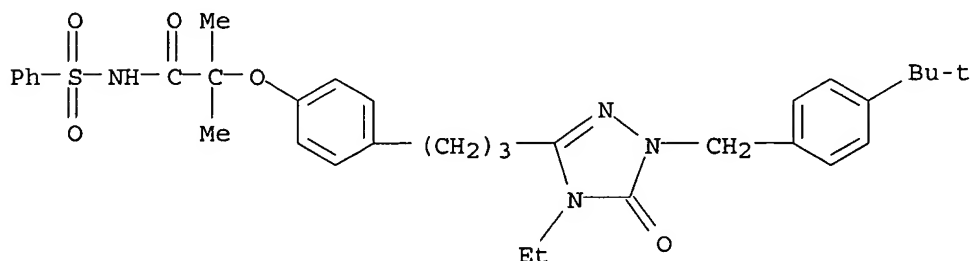
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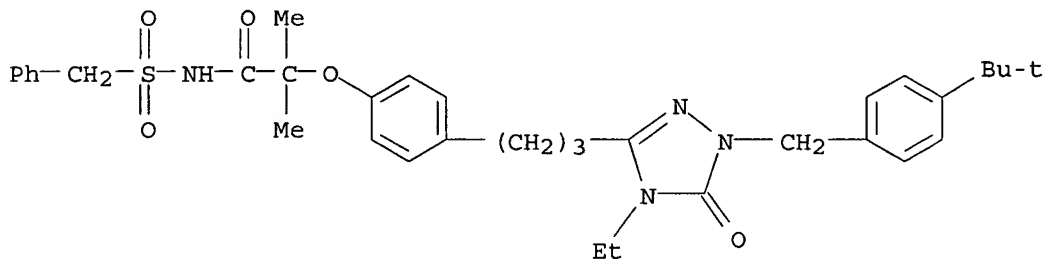
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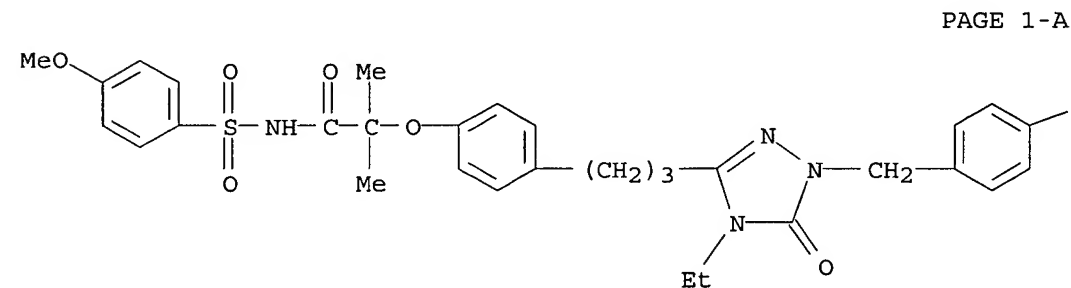
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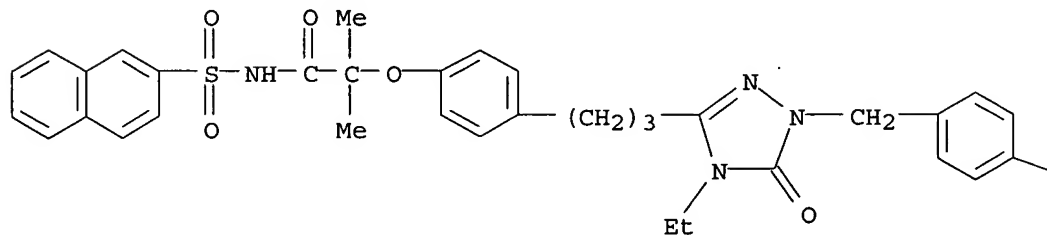
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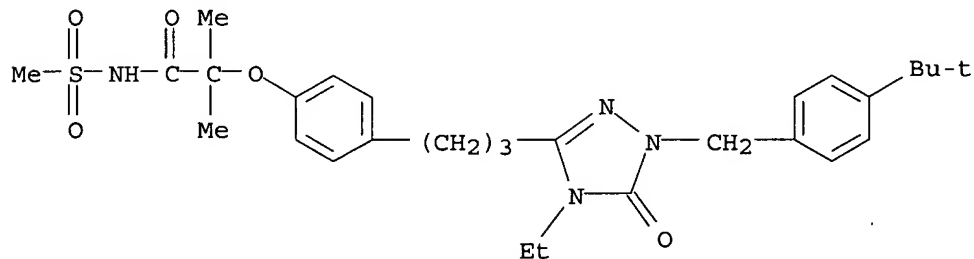
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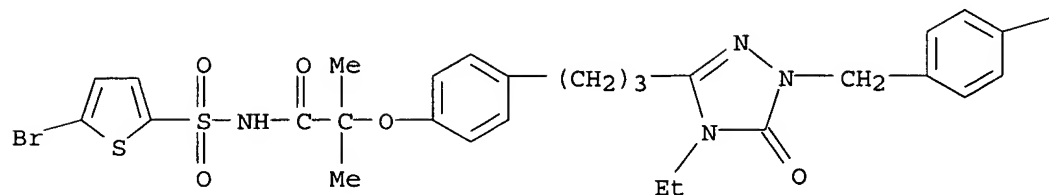
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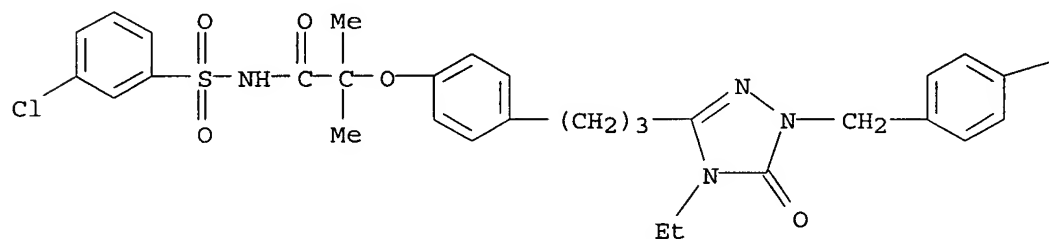
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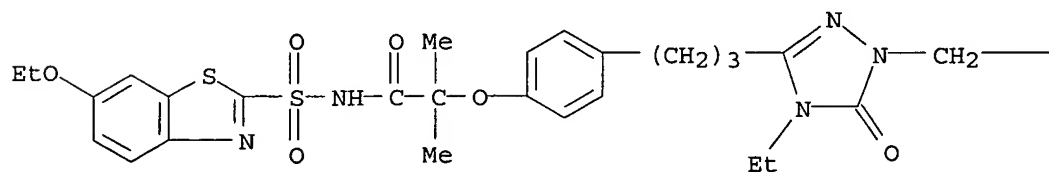
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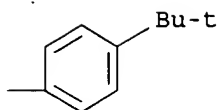
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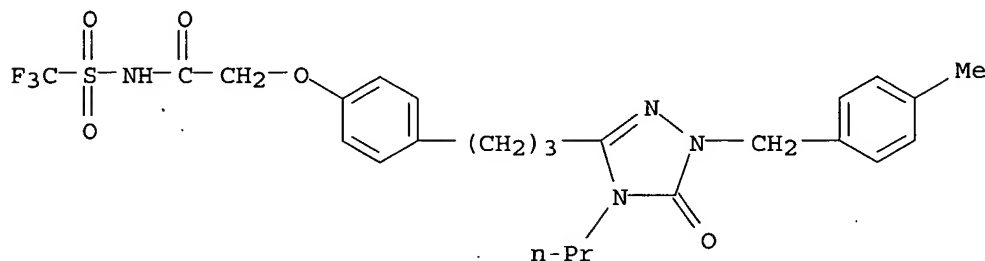
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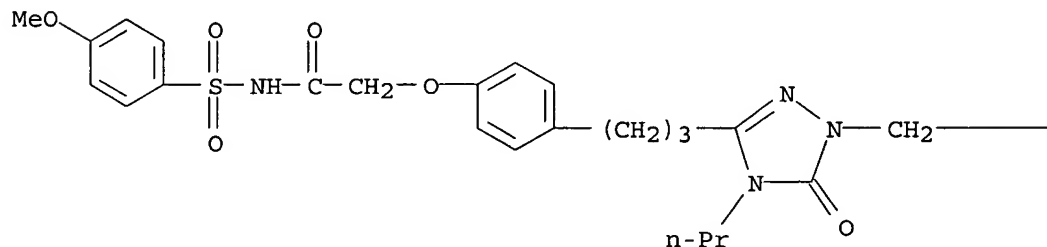
PAGE 1-B



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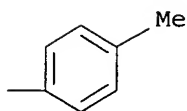


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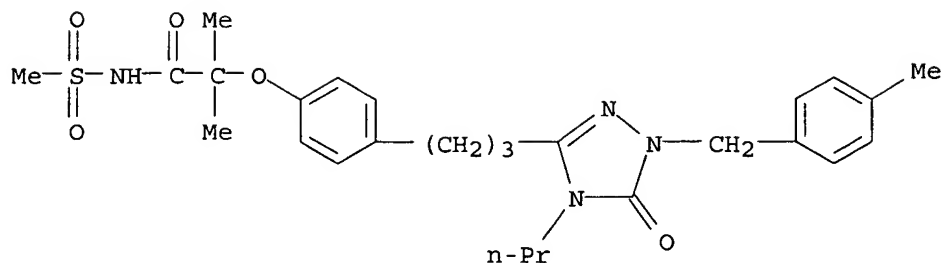


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		Section cross-reference(s): 1		
ST	phenylalkyl triazolone prepn	peroxisome proliferator		
		activated receptor alpha agonist; triazolone phenylalkyl prepn		
		Syndrome X treatment; triazolylalkylphenoxy propionate prepn		
		cardiovascular agents		
IT	Peroxisome proliferator-activated receptors			
		(α; preparation of (phenylalkyl)triazolones as PPARα		
		agonists for treatment of cardiovascular disease associated with		
		Syndrome X and related conditions)		
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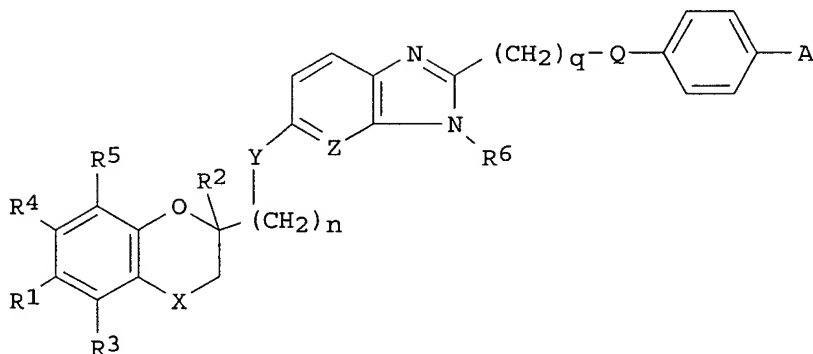
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 425672-29-3P 425672-30-6P

(cardiovascular agent; preparation of (phenylalkyl)triazolones as PPAR $\alpha$  agonists for treatment of cardiovascular disease associated with Syndrome X and related conditions)

L32 ANSWER 20 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2002:286703 HCAPLUS  
 DOCUMENT NUMBER: 136:309930

TITLE: Preparation of benzimidazole derivatives for treatment and prevention of **diabetes**  
 INVENTOR(S): Fujita, Takashi; Wada, Kunio; Koguchi, Minoru; Honma, Eiji; Fujiwara, Toshihiko  
 PATENT ASSIGNEE(S): Sankyo Co., Ltd., Japan  
 SOURCE: Jpn. Kokai Tokkyo Koho, 135 pp.  
 CODEN: JKXXAF  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2002114781	A2	20020416	JP 2000-307157	2000 1006
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PRIORITY APPLN. INFO.:			JP 2000-307157	2000 1006
			<--	
OTHER SOURCE(S):		MARPAT 136:309930		
GI				



AB The title compds. I [R1 - R6 = H, alkyl, etc.; n, q = 1 - 5; Q, Y = O, S; X = CH2, etc.; Z = CH, N; A = (CH2)mCH(CO2H)BR7, etc.; B = O, etc.; R7 = H, alkyl, etc.; m = 0 - 8] are prepared Compds. of this invention at 0.01% in feed (given for 3 days) gave 34.9% to 66.7% decrease of blood sugar in **diabetic** KK mice.

IT 300666-05-1P 300666-10-8P 300666-13-1P  
 300666-14-2P 300666-15-3P 300666-16-4P  
 300666-17-5P 300666-18-6P 300666-19-7P  
 300666-20-0P 300666-21-1P 300666-22-2P  
 300666-27-7P 300666-28-8P 300666-31-3P  
 (preparation of benzimidazole derivs. for treatment and prevention of **diabetes**)

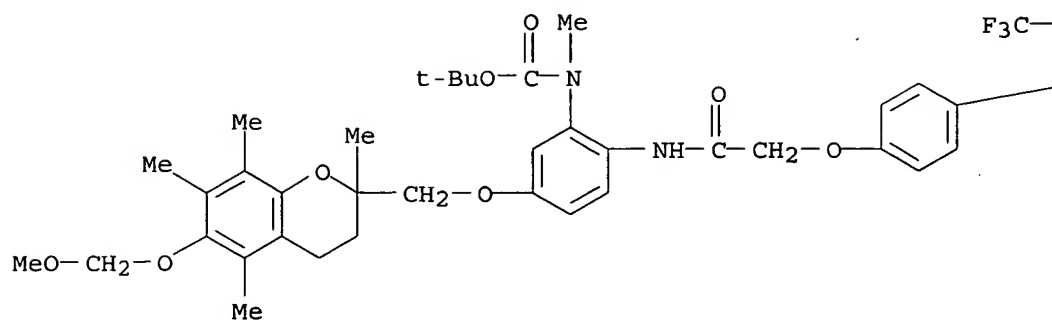
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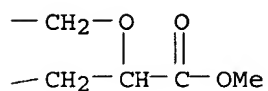


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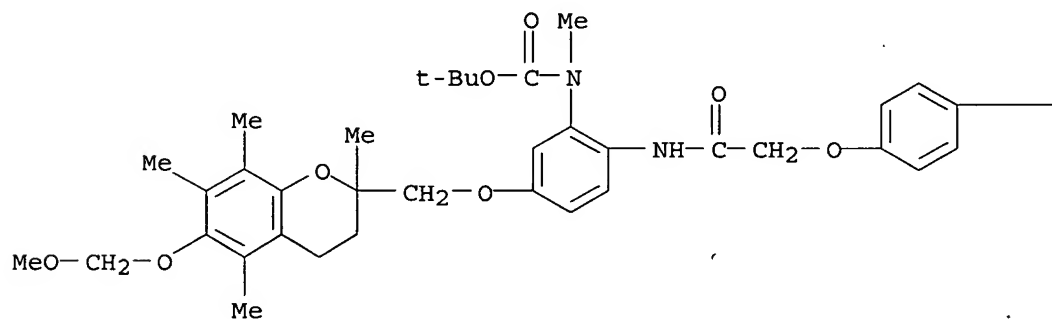


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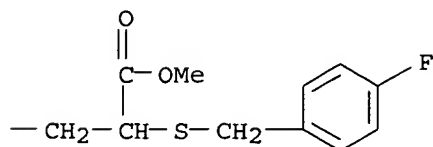


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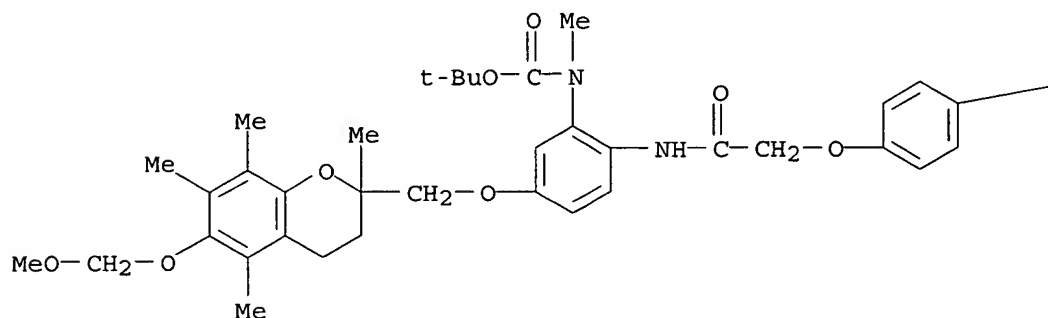
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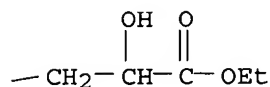
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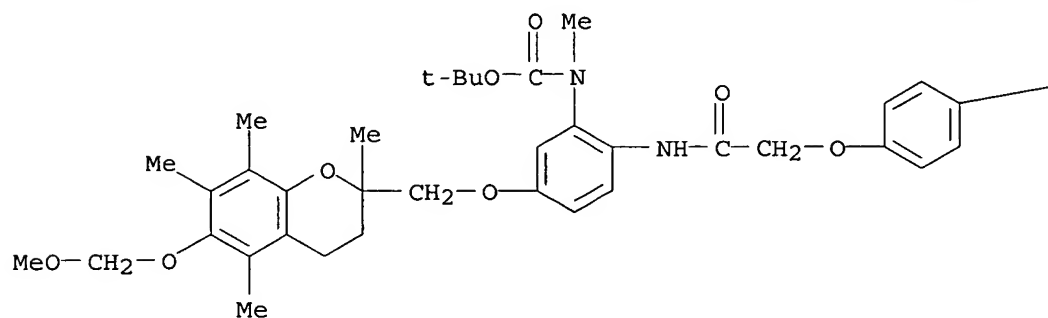
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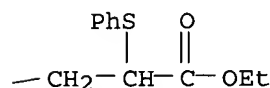
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PAGE 1-A

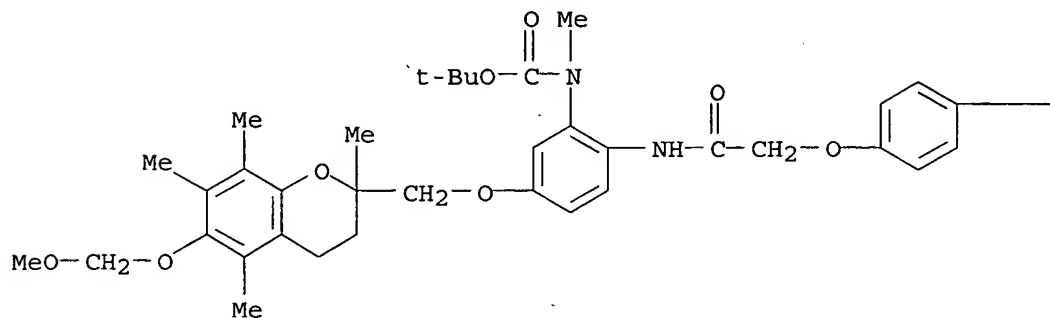


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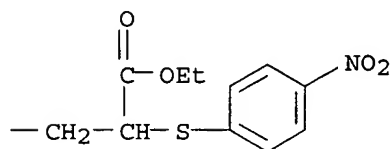


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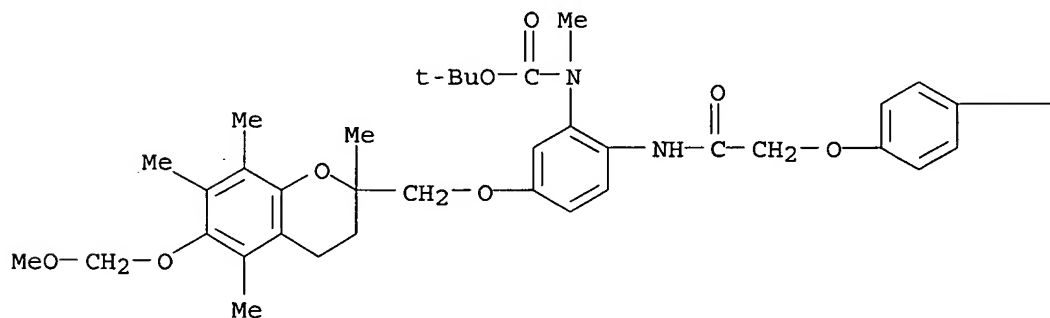


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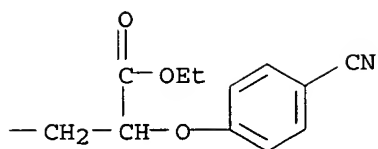


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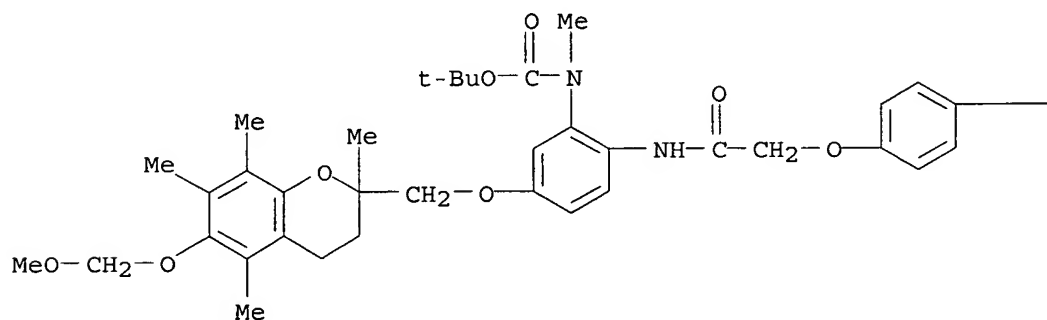
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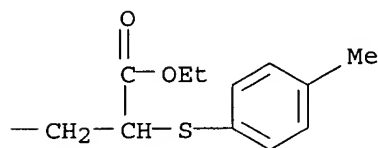
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PAGE 1-A



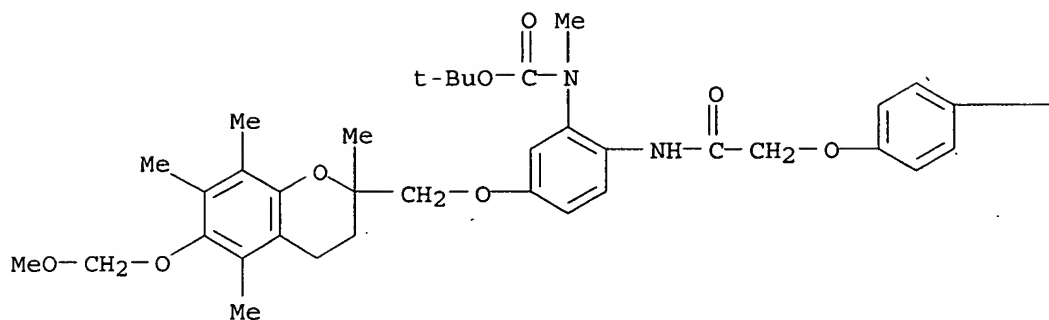
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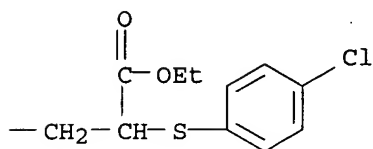
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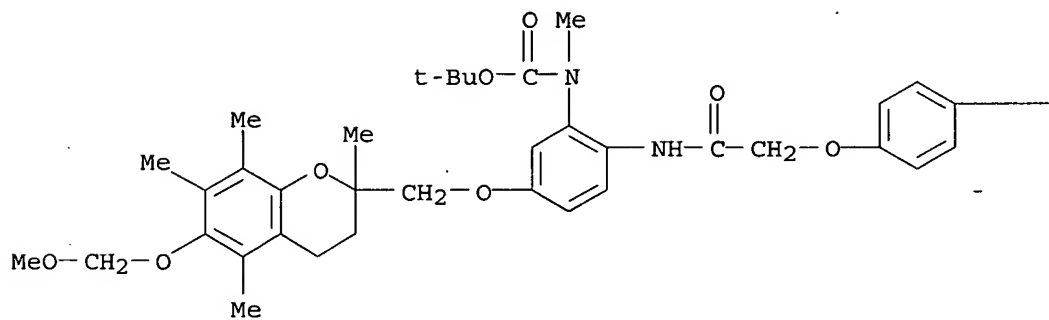
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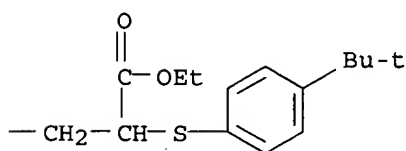
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(CA INDEX NAME)

PAGE 1-A

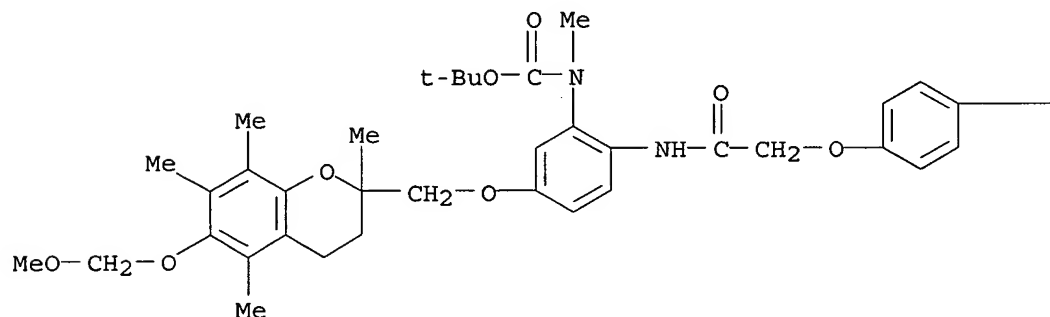


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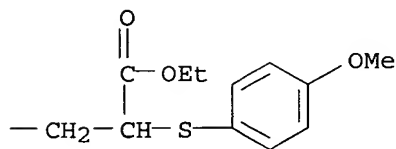


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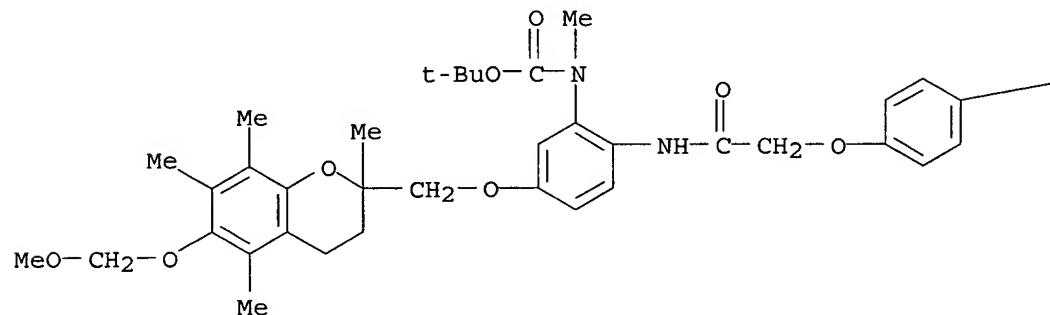


PAGE 1-B



RN 300666-21-1 HCAPLUS  
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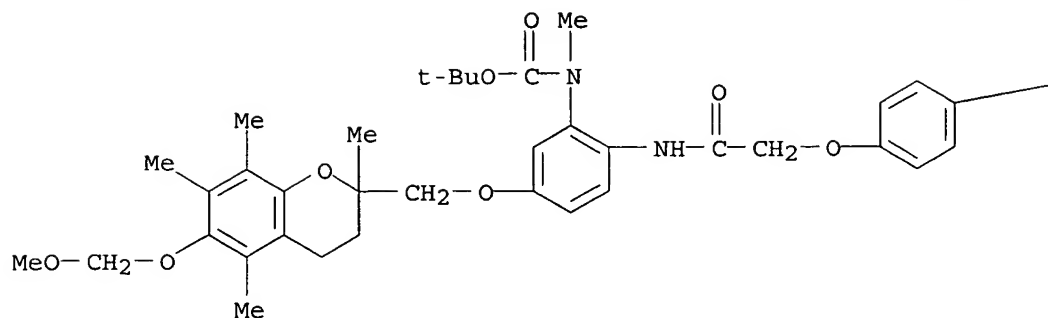
$$\begin{array}{c} \text{EtO} \quad \text{O} \\ | \quad || \\ -\text{CH}_2-\text{CH}-\text{C}-\text{OEt} \end{array}$$

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CN	Benzenepropanoic acid, 4-[2-[[4-[[3,4-dihydro-6-(methoxymethoxy)-2,5,7,8-tetramethyl-2H-1-benzopyran-2-yl]methoxy]-2-[[[(1,1-dimethylethoxy)carbonyl]methylamino]phenyl]amino]-2-oxoethoxy]- $\alpha$ -[(4-fluorophenyl)methoxy]-, ethyl ester (9CI) (CA INDEX NAME)	

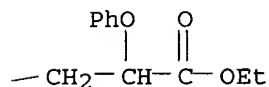
COCC1=C(C)C(OC)C(C)=C2C1OCC2COCc3ccc(NC(=O)COc4ccccc4)cc3N(C)C(=O)OC(C)(C)CCCOC(=O)C(COCc1ccc(F)cc1)CC

RN	300666-27-7	HCAPLUS
CN	Benzenepropanoic acid, 4-[2-[[4-[[3,4-dihydro-6-(methoxymethoxy)-2,5,7,8-tetramethyl-2H-1-benzopyran-2-yl]methoxy]-2-[[[(1,1-dimethylethoxy)carbonyl]methylamino]phenyl]amino]-2-oxoethoxy]- $\alpha$ -phenoxy-, ethyl ester (9CI) (CA INDEX NAME)	

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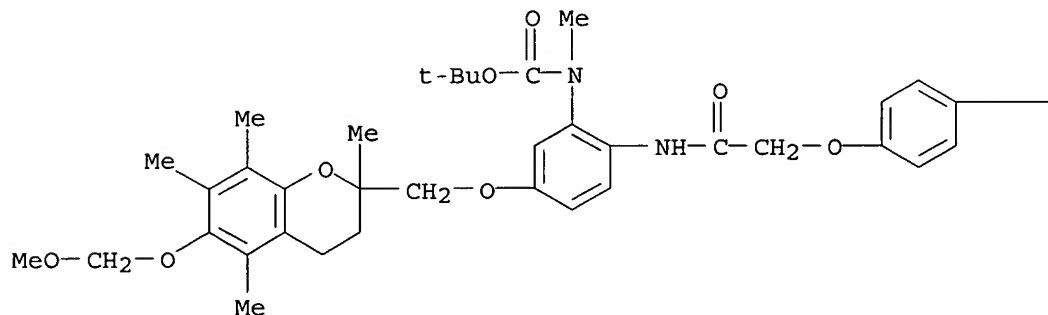
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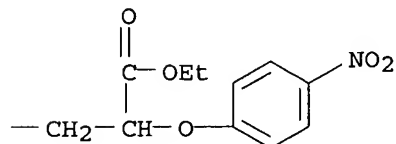
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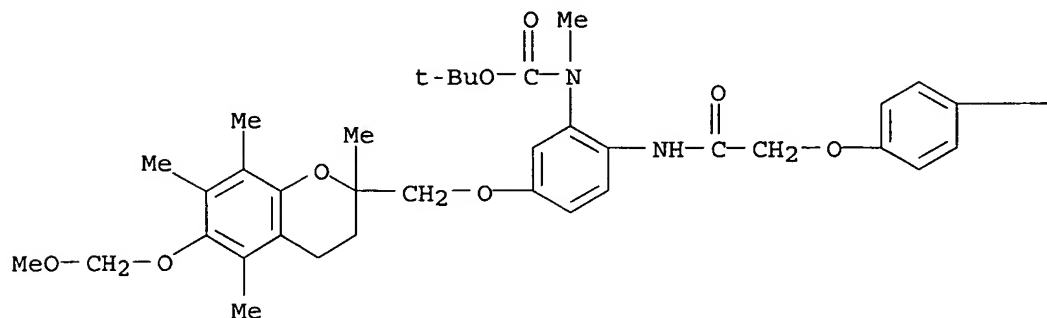


RN 300666-31-3 HCAPLUS

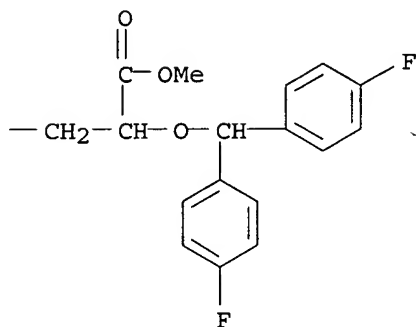
CN Benzenepropanoic acid,  $\alpha$ -[bis(4-fluorophenyl)methoxy]-4-[2-  
[[4-[[3,4-dihydro-6-(methoxymethoxy)-2,5,7,8-tetramethyl-2H-1-



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PAGE 1-B



USHA SHRESTHA EIC 1600 REM 1A64

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(preparation of benzimidazole derivs. for treatment and prevention of diabetes)

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(preparation of benzimidazole derivs. for treatment and prevention of diabetes)

IT 75-03-6, Ethyl iodide 93-03-8 100-02-7, 4-Nitrophenol, reactions 106-45-6 106-54-7, Benzenethiol, 4-chloro-108-95-2, Phenol, reactions 108-98-5, Thiophenol, reactions 306-23-0 459-46-1, 4-Fluorobenzyl bromide 593-56-6, O-Methylhydroxylamine hydrochloride 598-31-2, Bromoacetone 696-63-9, Benzenethiol, 4-methoxy- 767-00-0, 4-Cyanophenol 1849-36-1, 4-Nitrothiophenol 2396-68-1 2687-43-6, O-Benzylhydroxylamine hydrochloride 5292-43-3, tert-Butyl bromoacetate 5470-11-1, Hydroxylamine hydrochloride 27064-94-4, 4,4'-Difluorobenzhydryl chloride 66901-79-9 107188-55-6 107255-73-2 150556-71-1 156335-18-1 179087-93-5 299175-81-8 299176-17-3

(preparation of benzimidazole derivs. for treatment and prevention of diabetes)

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(preparation of benzimidazole derivs. for treatment and prevention of diabetes)

L32 ANSWER 21 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:237769 HCAPLUS

DOCUMENT NUMBER: 137:2321

TITLE: Investigation of Potential Bioisosteric Replacements for the Carboxyl Groups of Peptidomimetic Inhibitors of Protein Tyrosine Phosphatase 1B: Identification of a Tetrazole-Containing Inhibitor with Cellular Activity

AUTHOR(S): Liljebris, Charlotta; Larsen, Scott D.; Ogg, Derek; Palazuk, Barbara J.; Bleasdale, John E.

CORPORATE SOURCE: Departments of Medicinal Chemistry and

Structural Chemistry, Biovitrum AB, Uppsala,  
SE-751 82, Swed.  
SOURCE: Journal of Medicinal Chemistry (2002  
) , 45(9) , 1785-1798  
CODEN: JMCMAR; ISSN: 0022-2623  
PUBLISHER: American Chemical Society  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
OTHER SOURCE(S): CASREACT 137:2321

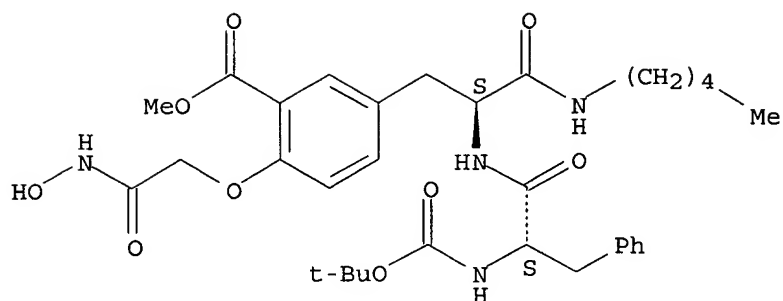
AB Protein tyrosine phosphatases (PTPs) constitute a diverse family of enzymes that, together with protein tyrosine kinases, control the level of intracellular tyrosine phosphorylation, thus regulating many cellular functions. PTP1B neg. regulates insulin signaling, in part, by dephosphorylating key tyrosine residues within the regulatory domain of the  $\beta$ -subunit of the insulin receptor, thereby attenuating receptor kinase activity. Inhibitors of PTP1B would therefore have the potential of prolonging the phosphorylated (activated) state of the insulin receptor and are anticipated to be a novel treatment of the insulin resistance characteristic of type 2 diabetes. We previously reported a series of small mol. weight peptidomimetics as competitive inhibitors of PTP1B, with the most active analogs having  $K_i$  values in the low nanomolar range. Furthermore, we confirmed that the O-carboxymethyl salicylic acid moiety is a remarkably effective novel phosphotyrosine mimetic. Because of the low cell permeability of this compound class, it was important to investigate the possibility of replacing one or both of the remaining carboxyl groups while maintaining PTP1B inhibitory activity. The analogs described herein further support the importance of an acidic functionality at both positions of the tyrosine head moiety. An important discovery was the ortho tetrazole analog 29 ( $K_i = 2.0 \mu\text{M}$ ), which was equipotent to the dicarboxylic acid analog 2 ( $K_i = 2.0 \mu\text{M}$ ). Solution of the x-ray cocrystal structure of the ortho tetrazole analog 29 bound to PTP1B revealed that the tetrazole moiety is well-accommodated in the active site and binds in a fashion similar to the ortho carboxylate analog 2 reported previously. This novel monocarboxylic acid analog revealed significantly higher Caco-2 cell permeability as compared to all previous compds. Furthermore, compound 29 exhibited modest enhancement of insulin-stimulated 2-deoxyglucose uptake by L6 myocytes.

IT 221077-60-7P  
(ortho tetrazole moiety replacements for carboxyl groups of peptidomimetic inhibitors of protein tyrosine phosphatase 1B can inhibit cellular activity)

RN 221077-60-7 HCAPLUS

CN L-Tyrosinamide, N-[(1,1-dimethylethoxy)carbonyl]-L-phenylalanyl-O-[2-(hydroxyamino)-2-oxoethyl]-3-(methoxycarbonyl)-N-pentyl- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.



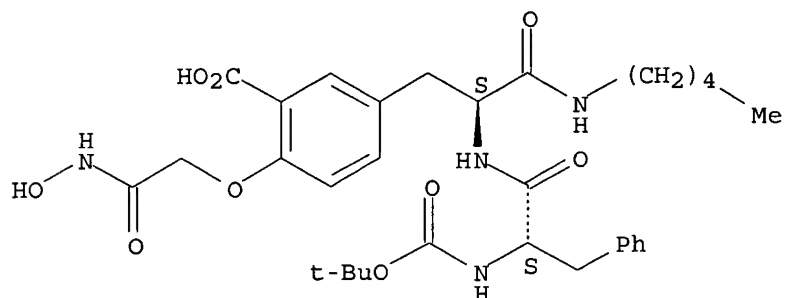
IT 221076-84-2P

(ortho tetrazole moiety replacements for carboxyl groups of peptidomimetic inhibitors of protein tyrosine phosphatase 1B can inhibit cellular activity)

RN 221076-84-2 HCAPLUS

CN L-Tyrosinamide, N-[(1,1-dimethylethoxy)carbonyl]-L-phenylalanyl-3-carboxy-O-[2-(hydroxyamino)-2-oxoethyl]-N-pentyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



CC 7-3 (Enzymes)

Section cross-reference(s): 1, 2, 75

IT **Diabetes mellitus**

(non-insulin-dependent; ortho tetrazole moiety replacements for carboxyl groups of peptidomimetic inhibitors of protein tyrosine phosphatase 1B can inhibit cellular activity)

IT **Antidiabetic agents**

Enzyme functional sites

Structure-activity relationship

(ortho tetrazole moiety replacements for carboxyl groups of peptidomimetic inhibitors of protein tyrosine phosphatase 1B can inhibit cellular activity)

IT 221077-52-7P 221077-59-4P 221077-60-7P 432551-05-8P

(ortho tetrazole moiety replacements for carboxyl groups of peptidomimetic inhibitors of protein tyrosine phosphatase 1B can inhibit cellular activity)

IT 221076-84-2P	221077-43-6P	221077-49-2P	221077-50-5P
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432551-15-0P

(ortho tetrazole moiety replacements for carboxyl groups of  
peptidomimetic inhibitors of protein tyrosine phosphatase 1B  
can inhibit cellular activity)

REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE  
FOR THIS RECORD. ALL CITATIONS AVAILABLE  
IN THE RE FORMAT

L32 ANSWER 22 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:185126 HCAPLUS

DOCUMENT NUMBER: 136:247485

TITLE: Preparation of bicyclic pyrrolyl amides as  
glycogen phosphorylase inhibitors

INVENTOR(S): Bartlett, Julie B.; Freeman, Sue; Kenny,  
Peter; Morley, Andrew; Whittamore, Paul

PATENT ASSIGNEE(S): Astrazeneca AB, Swed.

SOURCE: PCT Int. Appl., 141 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002020530	A1	20020314	WO 2001-SE1880	2001 0831

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GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG,  
KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK,  
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CA 2417594	AA	20020314	CA 2001-2417594	2001 0831
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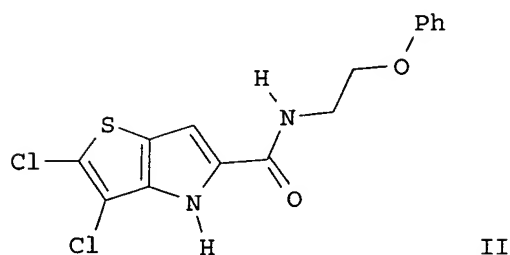
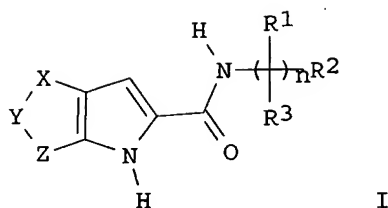
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OTHER SOURCE(S):	MARPAT 136:247485			
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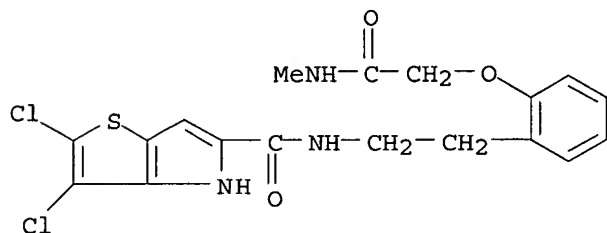
AB Title compds. I [R1 = H, halo, NO2, CN, OH, (un)substituted alkyl, alkenyl, etc.; R2 = H, halo, NO2, CH2F, CHF2, CF3, amino, alkyl, alkenyl, alkoxy, etc.; R3 = H, alkyl; -X-Y-Z- is selected from -S-CR4=CR5-, -CR4=CR5-S-, -O-CR4=CR5-, -CR4=CR5-O-, -N=CR4-S-, -S-CR4=N-, -NR3-CR4=CR5- and -CR4=CR5-NR3- wherein R4 and R5 = independently H, halo, CN, alkyl, ureido, NO2, etc.; n = 0-4] or a pharmaceutically acceptable salt or an in vivo hydrolyzable ester thereof were prepared possessing glycogen phosphorylase inhibitory activity (no data). Thus, II was prepared by amidation of 5-carboxy-2,3-dichloro-4H-thieno[3,2-b]pyrrole with 2-phenoxyethylamine. As glycogen phosphorylase inhibitors, I have value in the treatment of disease states associated with increased glycogen phosphorylase activity, e.g., type 2 **diabetes**. Pharmaceutical compns. containing I are described.

IT 403859-73-4P 403859-74-5P 403859-76-7P

(target compound; preparation of thienopyrrolyl amides as glycogen phosphorylase inhibitors)

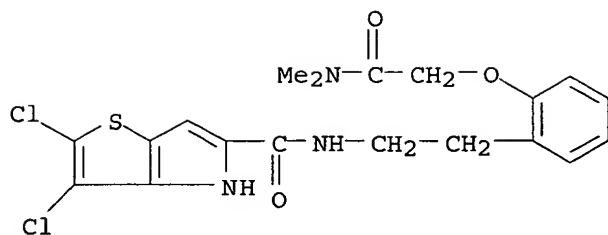
RN 403859-73-4 HCAPLUS

CN 4H-Thieno[3,2-b]pyrrole-5-carboxamide, 2,3-dichloro-N-[2-[2-(2-(methylamino)-2-oxoethoxy)phenyl]ethyl]- (9CI) (CA INDEX NAME)



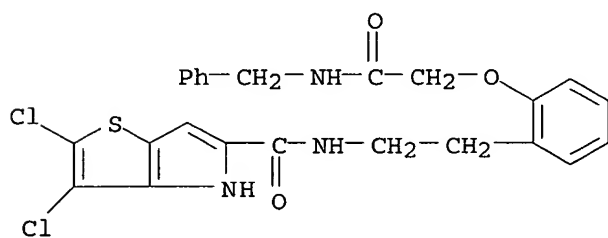
RN 403859-74-5 HCAPLUS

CN 4H-Thieno[3,2-b]pyrrole-5-carboxamide, 2,3-dichloro-N-[2-[2-(2-(dimethylamino)-2-oxoethoxy)phenyl]ethyl]- (9CI) (CA INDEX NAME)



RN 403859-76-7 HCAPLUS

CN 4H-Thieno[3,2-b]pyrrole-5-carboxamide, 2,3-dichloro-N-[2-[2-[2-oxo-2-[(phenylmethyl)amino]ethoxy]phenyl]ethyl]- (9CI) (CA INDEX NAME)



IC ICM C07D495-04

ICS C07D491-04; C07D513-04; C07D487-04; A61K031-407; A61P003-10; A61P009-10

CC 27-10 (Heterocyclic Compounds (One Hetero Atom))

Section cross-reference(s): 1, 34, 63

IT	403858-51-5P	403858-52-6P	403858-53-7P	403858-54-8P
	403858-55-9P	403858-56-0P	403858-57-1P	403858-58-2P
	403858-59-3P	403858-60-6P	403858-61-7P	403858-62-8P
	403858-63-9P	403858-64-0P	403858-65-1P	403858-66-2P
	403858-67-3P	403858-68-4P	403858-69-5P	403858-70-8P
	403858-71-9P	403858-72-0P	403858-73-1P	403858-74-2P
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 403860-78-6P 403860-79-7P 403860-80-0P

(target compound; preparation of thienopyrrolyl amides as glycogen phosphorylase inhibitors)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE  
 FOR THIS RECORD. ALL CITATIONS AVAILABLE  
 IN THE RE FORMAT

L32 ANSWER 23 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:185062 HCAPLUS

DOCUMENT NUMBER: 136:232548

TITLE: Preparation of  $\gamma$ -keto acid dipeptides as  
 inhibitors of caspase-3

INVENTOR(S): Han, Yongxin; Giroux, Andre; Grimm, Erich L.;  
 Aspiotis, Renee; Black, Cameron

PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.

SOURCE: PCT Int. Appl., 99 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002020465	A2	20020314	WO 2001-CA1272	2001 0906

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 GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG,  
 KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN,  
 MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI,  
 SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA,  
 ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE,  
 CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,  
 PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,  
 MR, NE, SN, TD, TG

CA 2421172	AA	20020314	CA 2001-2421172	2001 0906
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AU 2001093533	A5	20020322	AU 2001-93533	2001 0906
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EP 1317414 A2 20030611 EP 2001-973867  
2001  
0906

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,  
MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR  
JP 2004521080 T2 20040715 JP 2002-525088  
2001  
0906

US 2002165230 A1 20021107 US 2001-948244  
2001  
0907

US 6525025 B2 20030225  
PRIORITY APPLN. INFO.: US 2000-231019P P  
2000  
0908

WO 2001-CA1272 W  
2001  
0906

OTHER SOURCE(S): MARPAT 136:232548

AB  $\gamma$ -Keto acid dipeptides RCR<sub>1</sub>2CONHCR<sub>2</sub>R<sub>3</sub>CONHCH(CH<sub>2</sub>CO<sub>2</sub>H)COCH<sub>2</sub>-O-W-Z [W = a bond, CH<sub>2</sub>, CO or COCH<sub>2</sub>; Z = H, (un)substituted alkyl, cycloalkyl or a benzofused analog, Ph, naphthyl or a 5- to 10-membered mono- or bicyclic, aromatic or non-aromatic ring, or a benzofused analog, containing 1-3 heteroatoms selected from O, S and N; R = (un)substituted alkoxyphenyl; R<sub>1</sub> = H, halo, OH, alkyl or alkoxy optionally substituted by oxo or 1-3 halo groups; R<sub>2</sub> = H, Ph, naphthyl, (un)substituted (cyclo)alkyl; R<sub>3</sub> = H or R<sub>2</sub>R<sub>3</sub> represent a 4-7 membered ring optionally containing one heteroatom selected from O, S and N] were prepared as inhibitors of caspase-3. Thus, (3S)-5-[(2-chloro-6-fluorobenzyl)oxy]-3-[[[(2S)-2-[[2-(2,5-dimethoxyphenyl)acetyl]amino]-3-methylbutanoyl]amino]-4-oxopentanoic acid was prepared by the solid phase method by loading (S)-FmocNHCH(CH<sub>2</sub>CO<sub>2</sub>Bu-t)COCH<sub>2</sub>Br (Fmoc = fluorenylmethoxycarbonyl) (preparation described) onto a solid support using the technol. described by Webb et al. (1992).

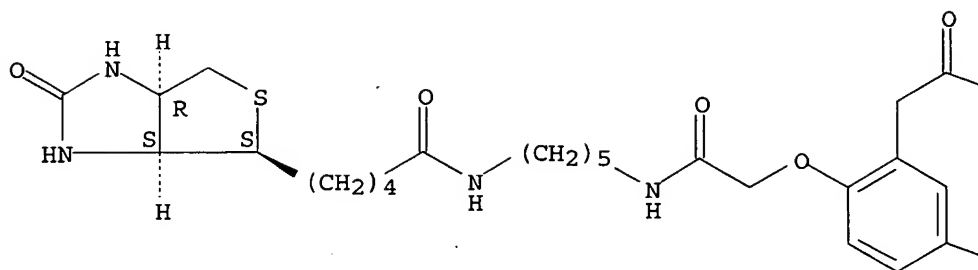
IT 403499-31-0P  
(preparation of  $\gamma$ -keto acid dipeptides as inhibitors of caspase-3)

RN 403499-31-0 HCAPLUS

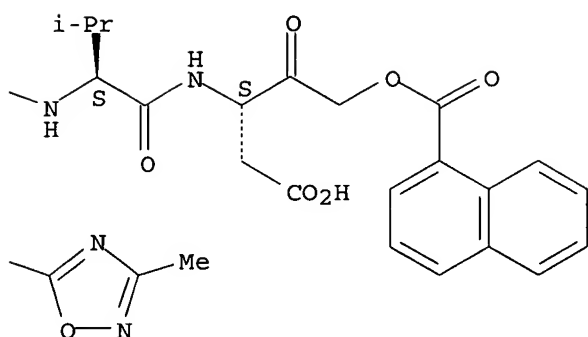
CN 1-Naphthalenecarboxylic acid, (3S)-4-carboxy-3-[[[(2S)-2-[[[2-[2-[[5-[5-[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]amino]pentyl]amino]-2-oxoethoxy]-5-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl]acetyl]amino]-3-methyl-1-oxobutyl]amino]-2-oxobutyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



IT 403499-96-7P 403499-97-8P

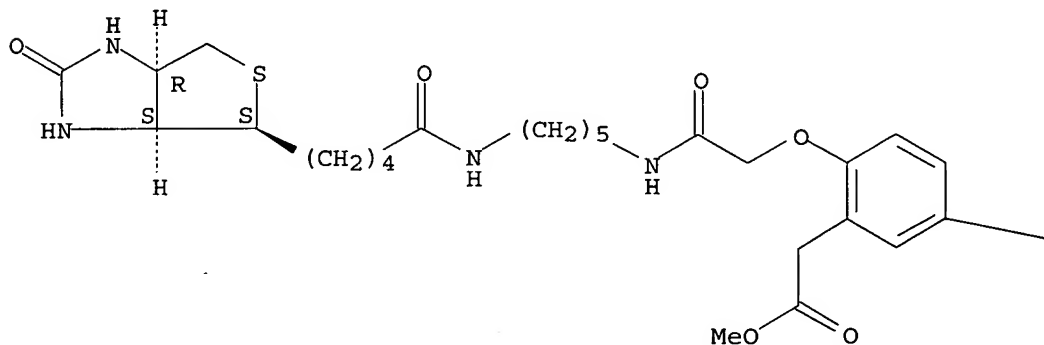
(preparation of  $\gamma$ -keto acid dipeptides as inhibitors of caspase-3)

RN 403499-96-7 HCAPLUS

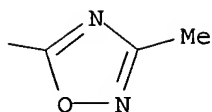
CN Benzeneacetic acid, 2-[2-[[5-[[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]amino]pentyl]amino]-2-oxoethoxy]-5-(3-methyl-1,2,4-oxadiazol-5-yl)-, methyl ester (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

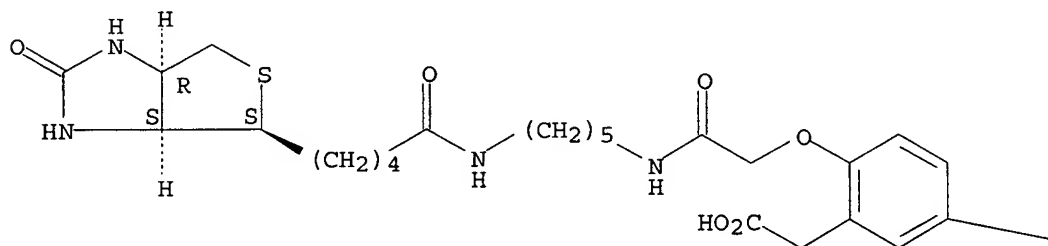


RN 403499-97-8 HCAPLUS

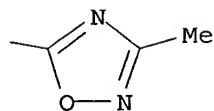
CN Benzeneacetic acid, 2-[2-[[5-[[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]amino]pentyl]amino]-2-oxoethoxy]-5-(3-methyl-1,2,4-oxadiazol-5-yl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



IC ICM C07C237-22

ICS A61K031-16; A61P031-18; C07D413-12; C07D241-44; C07D239-34;  
C07D307-86

CC 34-3 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 1, 7

IT Autoimmune disease

(insulin-dependent **diabetes** mellitus; preparation of  
γ-keto acid dipeptides as inhibitors of caspase-3)

IT **Diabetes** mellitus

(insulin-dependent; preparation of  $\gamma$ -keto acid dipeptides as inhibitors of caspase-3)

IT	403499-16-1P	403499-17-2P	403499-18-3P	403499-19-4P
	403499-20-7P	403499-21-8P	403499-22-9P	403499-23-0P
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	403499-28-5P	403499-29-6P	403499-30-9P	403499-31-0P
	403499-32-1P	403499-33-2P	403499-34-3P	403499-35-4P
	403499-36-5P	403499-37-6P	403499-38-7P	403499-39-8P
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	403499-80-9P	403499-81-0P	403499-82-1P	403499-83-2P

(preparation of  $\gamma$ -keto acid dipeptides as inhibitors of caspase-3)

IT	116296-30-1P	294860-44-9P	294860-95-0P	294860-96-1P
	403499-86-5P	403499-87-6P	403499-88-7P	403499-89-8P
	403499-90-1P	403499-91-2P	403499-94-5P	403499-95-6P
	403499-96-7P	403499-97-8P		

(preparation of  $\gamma$ -keto acid dipeptides as inhibitors of caspase-3)

L32 ANSWER 24 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:704703 HCAPLUS

DOCUMENT NUMBER: 135:257231

TITLE: Preparation of catechol propionic acid derivatives as peroxisome proliferator-activated receptor (PPAR)  $\alpha$  and  $\gamma$  agonists

INVENTOR(S): Kadota, Hidetoshi; Fukazawa, Nobuyuki; Maruyama, Kyoko; Nakao, Toshifumi; Asada, Noriaki; Takebayashi, Nozomi; Kibayashi, Kenji; Uda, Hideyuki; Morikawa, Maki

PATENT ASSIGNEE(S): Mitsui Chemicals Inc., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 21 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

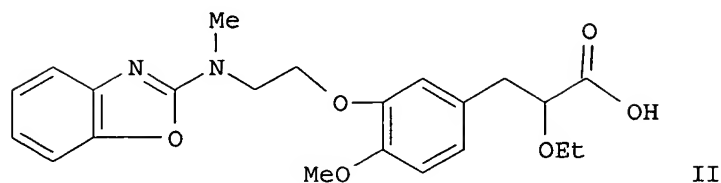
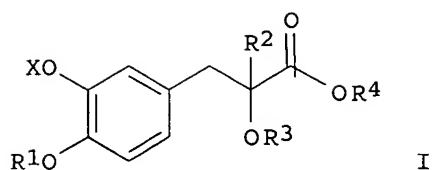
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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JP 2001261612	A2	20010926	JP 2000-79220	2000 0322

PRIORITY APPLN. INFO.:	<--	JP 2000-79220	2000 0322
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OTHER SOURCE(S): MARPAT 135:257231

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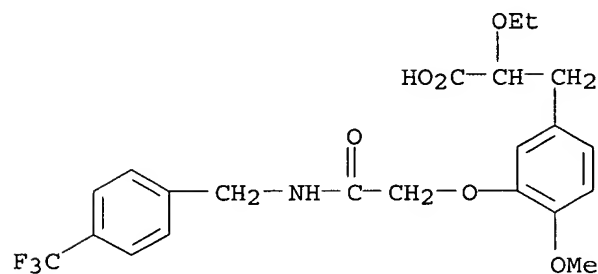


AB The title compds. I [R1 = alkyl, etc.; R2 = H, alkoxy, etc.; R3 = H, alkyl, etc.; R4 = H, alkyl, etc.; X = (un)substituted Ph, etc.] are prepared The PPAR  $\alpha$  and  $\gamma$  agonist activities of the title compound II were demonstrated; II at 100 mg/kg gave 16% blood sugar decrease in STZ mice.

IT **362012-80-4P**  
(preparation of catechol propionic acid derivs. as  
peroxisome proliferator-activated receptor  $\alpha$  and  
 $\gamma$  agonists)

RN 362012-80-4 HCAPLUS

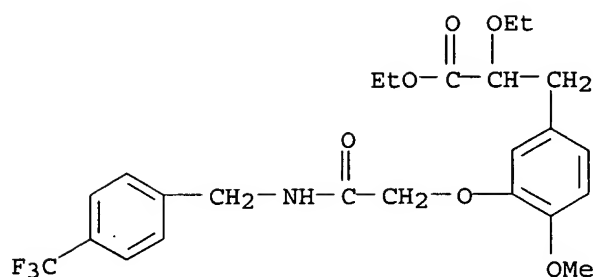
CN Benzenepropanoic acid,  $\alpha$ -ethoxy-4-methoxy-3-[2-oxo-2-[[[4-(trifluoromethyl)phenyl]methyl]amino]ethoxy]- (9CI) (CA INDEX NAME)



IT **362012-94-0P**  
(preparation of catechol propionic acid derivs. as  
peroxisome proliferator-activated receptor  $\alpha$  and  
 $\gamma$  agonists)

RN 362012-94-0 HCAPLUS

CN Benzenepropanoic acid,  $\alpha$ -ethoxy-4-methoxy-3-[2-oxo-2-[[[4-(trifluoromethyl)phenyl]methyl]amino]ethoxy]-, ethyl ester (9CI) (CA INDEX NAME)



- IC ICM C07C059-13  
 ICS A61K031-192; A61K031-195; A61K031-216; A61K031-275;  
 A61K031-381; A61K031-423; A61P001-00; A61P001-04; A61P001-16;  
 A61P003-06; A61P003-10; A61P007-00; A61P009-10; A61P011-00;  
 A61P011-06; A61P029-00; A61P031-06; A61P031-18; A61P035-00
- CC 28-6 (Heterocyclic Compounds (More Than One Hetero Atom))  
 Section cross-reference(s): 1, 25
- ST PPAR agonist **antidiabetic** catechol propionate prepn;  
 benzoxazolylaminoethoxyphenylpropanoic acid prepn PPAR agonist  
**antidiabetic**
- IT Intestine, disease  
 (Crohn's; preparation and effect of catechol propionic acid derivs.  
 with **peroxisome** proliferator-activated receptor  
 agonist activity)
- IT Bronchi  
 (bronchitis; preparation and effect of catechol propionic acid  
 derivs. with **peroxisome** proliferator-activated  
 receptor agonist activity)
- IT Allergy inhibitors  
 Antiasthmatics  
**Antidiabetic** agents  
 Hypolipemic agents  
 (catechol propionic acid derivs. with **peroxisome**  
 proliferator-activated receptor agonist activity)
- IT Malaria  
 (cerebral; preparation and effect of catechol propionic acid derivs.  
 with **peroxisome** proliferator-activated receptor  
 agonist activity)
- IT Brain, disease  
 (malaria; preparation and effect of catechol propionic acid derivs.  
 with **peroxisome** proliferator-activated receptor  
 agonist activity)
- IT Arteriosclerosis  
 Arthritis  
 Autoimmune disease  
 Hepatitis  
 Multiple sclerosis  
 Osteoarthritis  
 (preparation and effect of catechol propionic acid derivs. with  
**peroxisome** proliferator-activated receptor agonist  
 activity)
- IT **Peroxisome** proliferator-activated receptors  
 (preparation of catechol propionic acid derivs. as  
**peroxisome** proliferator-activated receptor  $\alpha$  and  
 $\gamma$  agonists)
- IT Shock (circulatory collapse)  
 (septic; preparation and effect of catechol propionic acid derivs.)

with **peroxisome** proliferator-activated receptor agonist activity)

IT Intestine, disease  
(ulcerative colitis; preparation and effect of catechol propionic acid derivs. with **peroxisome** proliferator-activated receptor agonist activity)

IT Infection  
(viral; preparation and effect of catechol propionic acid derivs. with **peroxisome** proliferator-activated receptor agonist activity)

IT 362012-74-6P 362012-75-7P 362012-76-8P 362012-77-9P  
362012-78-0P 362012-79-1P **362012-80-4P** 362012-81-5P  
362012-82-6P 362012-83-7P  
(preparation of catechol propionic acid derivs. as **peroxisome** proliferator-activated receptor  $\alpha$  and  $\gamma$  agonists)

IT 402-49-3, 4-Trifluoromethylbenzyl bromide 455-24-3,  
4-Trifluoromethylbenzoic acid 817-95-8, Ethyl ethoxyacetate  
3300-51-4, 4-Trifluoromethylbenzylamine 5292-43-3, tert-Butyl  
bromoacetate 6346-05-0, 3-Benzyloxy-4-methoxybenzaldehyde  
23046-03-9 26690-80-2, N-tert-Butoxycarbonyl-2-aminoethanol  
40786-20-7 67387-76-2, 3-Cyclopentyloxy-4-methoxybenzaldehyde  
122320-77-8 184879-05-8 227029-27-8 343870-73-5  
362013-01-2 362013-02-3  
(preparation of catechol propionic acid derivs. as **peroxisome** proliferator-activated receptor  $\alpha$  and  $\gamma$  agonists)

IT 362012-84-8P 362012-85-9P 362012-86-0P 362012-87-1P  
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362012-92-8P 362012-93-9P **362012-94-0P** 362012-95-1P  
362012-96-2P 362012-97-3P 362012-98-4P 362012-99-5P  
362013-00-1P  
(preparation of catechol propionic acid derivs. as **peroxisome** proliferator-activated receptor  $\alpha$  and  $\gamma$  agonists)

L32 ANSWER 25 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:152692 HCAPLUS

DOCUMENT NUMBER: 134:193424

TITLE: Preparation of oxazoloisindole derivatives  
and analogs as remedies for **diabetes**  
(or complications thereof) and obesity

INVENTOR(S): Nagase, Toshio; Iino, Tomoharu; Sato,  
Yoshiyuki; Nishimura, Teruyuki; Eiki, Jun-ichi

PATENT ASSIGNEE(S): Banyu Pharmaceutical Co., Ltd., Japan

SOURCE: PCT Int. Appl., 322 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2001014386	A1	20010301	WO 2000-JP5723	2000 0825

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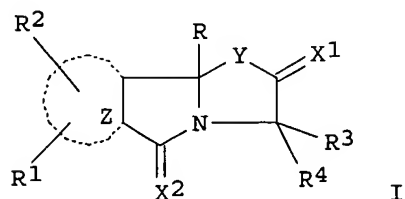


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OTHER SOURCE(S):  
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MARPAT 134:193424



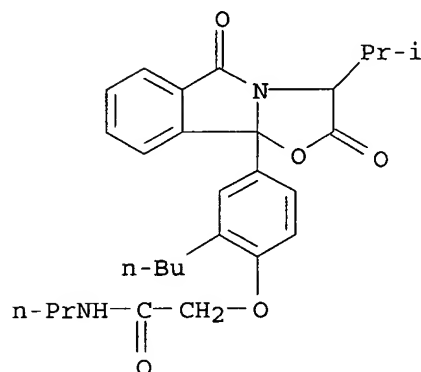
AB The title compds. I [R represents azido, etc.; R1 and R2 are the same or different and each represents hydrogen, etc.; R3 and R4 are the same or different and each represents hydrogen, etc.; X1 represents oxygen, etc.; X2 represents oxygen, etc.; Y represents oxygen, etc.; and Z represents fused aryl, etc.] are prepared. The title compound I [R1 = R2 = R4 = H; R3 = isopropyl; Z = phenyl; R = phenyl] at 30 mg/kg significantly increased the concentration of GLP-1 in plasma in rats. Formulations are given.

IT 327599-44-0P

(preparation of oxazoloisoindole derivs. and analogs as remedies for **diabetes** (or complications thereof) and obesity)

RN 327599-44-0 HCAPLUS

CN Acetamide, 2-[2-butyl-4-[2,3-dihydro-3-(1-methylethyl)-2,5-dioxooxazolo[2,3-a]isoindol-9b(5H)-yl]phenoxy]-N-propyl- (9CI)  
(CA INDEX NAME)



IC ICM C07D491-048

ICS C07D491-147; C07D487-04; C07D471-14; C07D487-14; C07D513-04;  
C07D513-14; C07D498-14; C07D498-04; A61K031-424; A61K031-437;  
A61K031-4188; A61K031-4985; A61K031-407; A61K031-519;  
A61K031-5377; A61K031-4439; A61K031-429; A61K031-5025;  
A61P003-10

CC 28-6 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1, 34, 63

ST oxazoloisoindole prepn **diabetes** obesity remedy

IT **Diabetes** mellitus

Obesity

(preparation of oxazoloisoindole derivs. and analogs as remedies for **diabetes** (or complications thereof) and obesity)

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(preparation of oxazoloisoindole derivs. and analogs as remedies for diabetes (or complications thereof) and obesity)

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(preparation of oxazoloisindole derivs. and analogs as remedies for  
**diabetes** (or complications thereof) and obesity)

IT 89750-14-1, Glucagon-like peptide I

(preparation of oxazoloisindole derivs. and analogs as remedies for  
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IT 75-16-1, Methylmagnesium bromide 85-52-9, 2-Benzoylbenzoic acid

88-99-3, Phthalic acid, reactions 578-57-4, 2-Bromoanisole

1151-15-1, 2-(4-Methoxybenzoyl)benzoic acid 6638-79-5,

N,O-Dimethylhydroxylamine hydrochloride 7146-15-8, D-Valine

methyl ester hydrochloride 7664-41-7, Ammonia, reactions

16721-80-5, Sodium hydrogen sulfide 22838-58-0,

N-tert-Butoxycarbonyl-D-valine

(preparation of oxazoloisindole derivs. and analogs as remedies for  
**diabetes** (or complications thereof) and obesity)

IT 1151-04-8P 70717-76-9P, N-tert-Butoxycarbonyl-D-valine amide

190260-92-5P 327600-47-5P 327600-48-6P 327600-49-7P

327600-50-0P

(preparation of oxazoloisindole derivs. and analogs as remedies for  
**diabetes** (or complications thereof) and obesity)

REFERENCE COUNT:

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THERE ARE 28 CITED REFERENCES AVAILABLE  
FOR THIS RECORD. ALL CITATIONS AVAILABLE  
IN THE RE FORMAT

L32 ANSWER 26 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:742095 HCAPLUS

DOCUMENT NUMBER: 133:296438

TITLE: Preparation of substituted fused imidazole  
derivatives as hypoglycemics

INVENTOR(S): Fujita, Takashi; Wada, Kunio; Oguchi, Minoru;  
Honma, Hidehito; Fujiwara, Toshihiko

PATENT ASSIGNEE(S): Sankyo Company, Ltd., Japan

SOURCE: PCT Int. Appl., 274 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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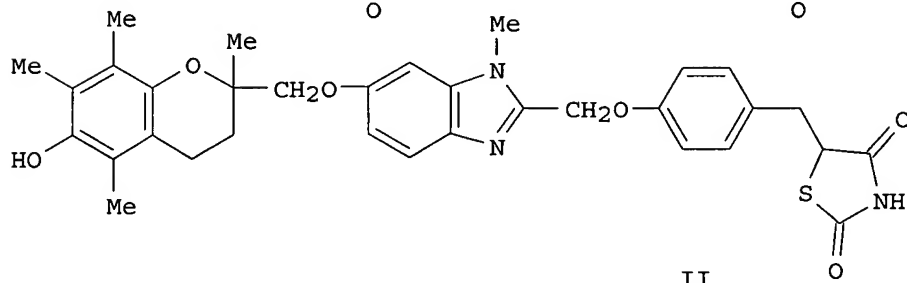
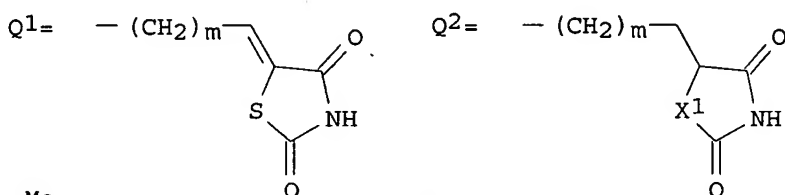
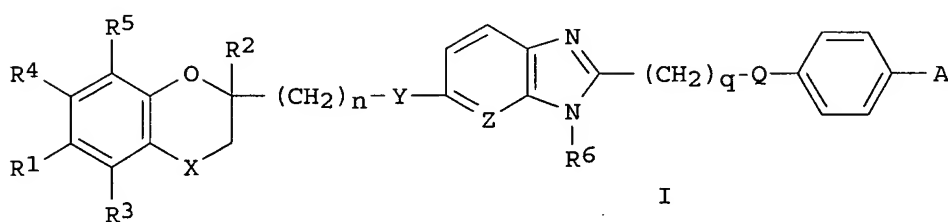
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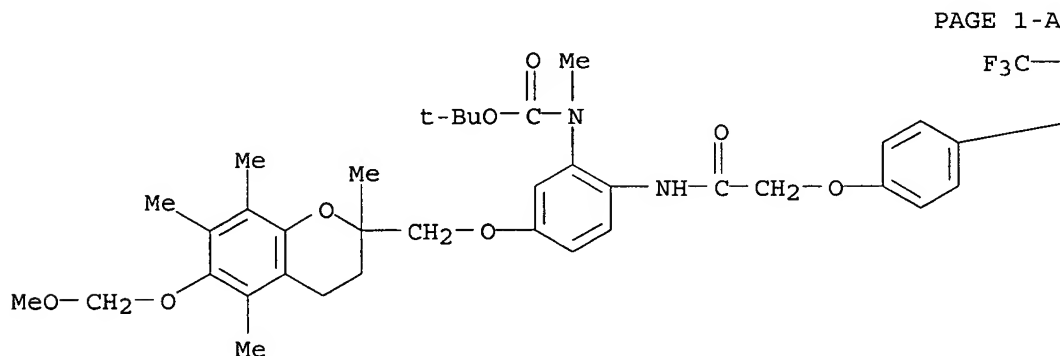
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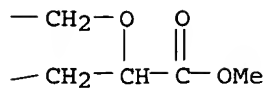


AB Compds. represented by general formula (I) and salts and esters thereof [wherein R1 is hydrogen, C1-6 alkyl, (un)substituted C6-10 aryl or C7-16 aralkyl, HO, (un)substituted acyloxy, C1-6 alkoxy, (un)substituted NH2, etc.; R2 is hydrogen, C1-6 alkyl, or (un)substituted C7-16 aralkyl; R4, R4, or R5 is each hydrogen, C1-6 alkyl, or C1-6 alkoxy; R6 is hydrogen, C1-6 alkyl, (un)substituted C6-10 aryl or C7-16 aralkyl; Q and Y are each oxygen or sulfur; X is CH2, CO, CH(OR9), or C(:NOR10); wherein R9 or R10 is hydrogen, (un)substituted C1-6 alkyl, C7-16 aralkyl, or acyl; Z is CH or nitrogen; n and q are each 1 to 5; and A is a group represented by general formula Q1, Q2, Q3, or (CH2)m CH(CO2H)-BR7; wherein m is 0 to 8; X1 is oxygen or sulfur; B is oxygen, sulfur, or (un)substituted NH; and R7 is hydrogen, C1-6 alkyl, (un)substituted C6-10 aryl or C7-16 aralkyl, or haloalkyl]

IT	300666-05-1P 300666-10-8P 300666-13-1P 300666-14-2P 300666-15-3P 300666-16-4P 300666-17-5P 300666-18-6P 300666-19-7P 300666-20-0P 300666-21-1P 300666-22-2P 300666-27-7P 300666-28-8P 300666-31-3P (preparation of substituted fused imidazole derivs. as therapeutics)
RN	300666-05-1 HCAPLUS
CN	Benzenepropanoic acid, 4-[2-[[4-[[3,4-dihydro-6-(methoxymethoxy)- 2,5,7,8-tetramethyl-2H-1-benzopyran-2-yl]methoxy]-2-[[[(1,1- dimethylethoxy)carbonyl]methylamino]phenyl]amino]-2-oxoethoxy]- α-(2,2,2-trifluoroethoxy)-, methyl ester (9CI) (CA INDEX NAME)



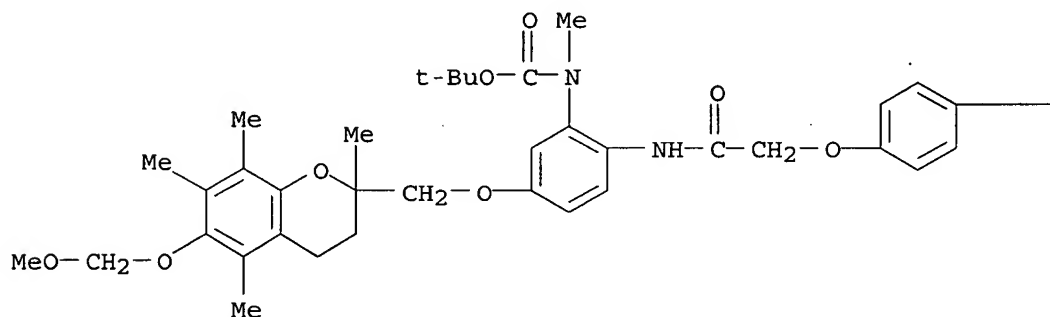
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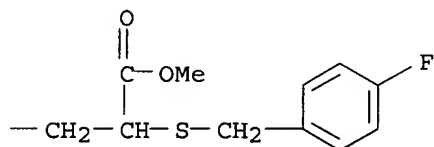
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PAGE 1-A



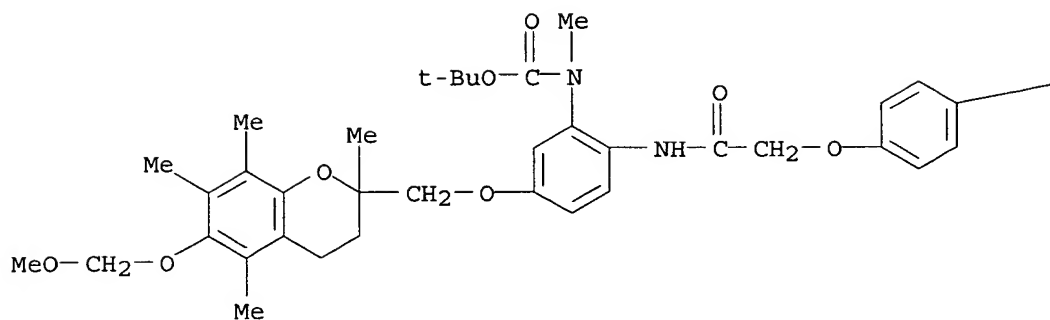
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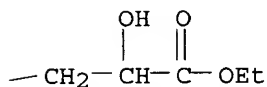
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PAGE 1-A



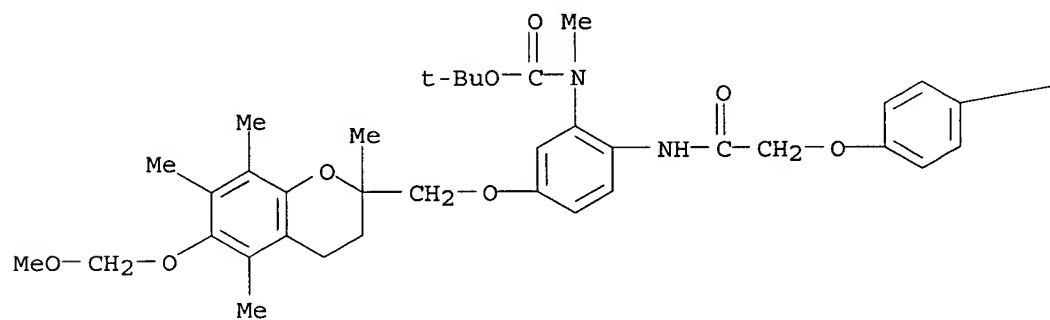
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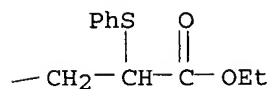
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PAGE 1-A



PAGE 1-B



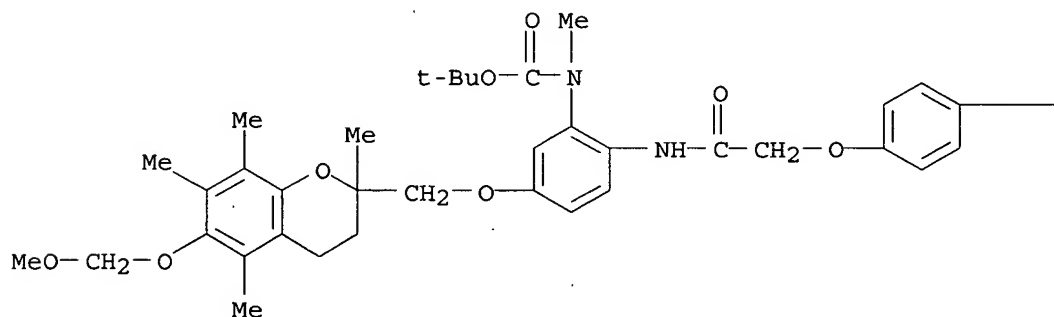
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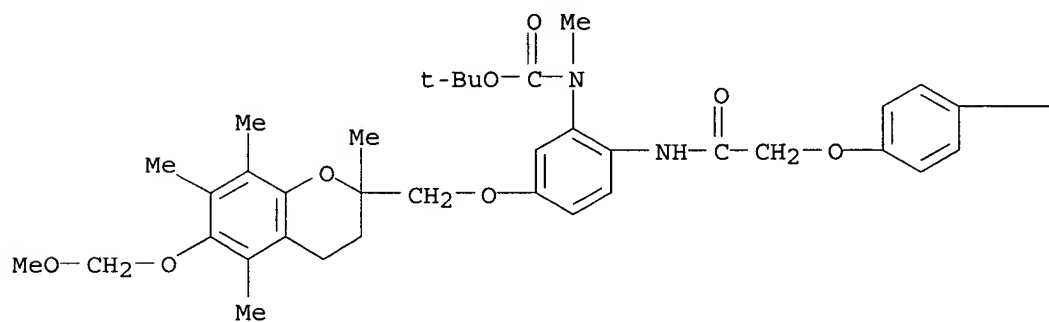
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PAGE 1-A

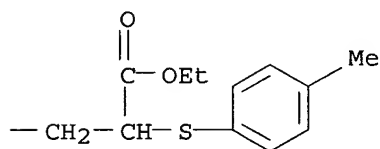
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PAGE 1-A

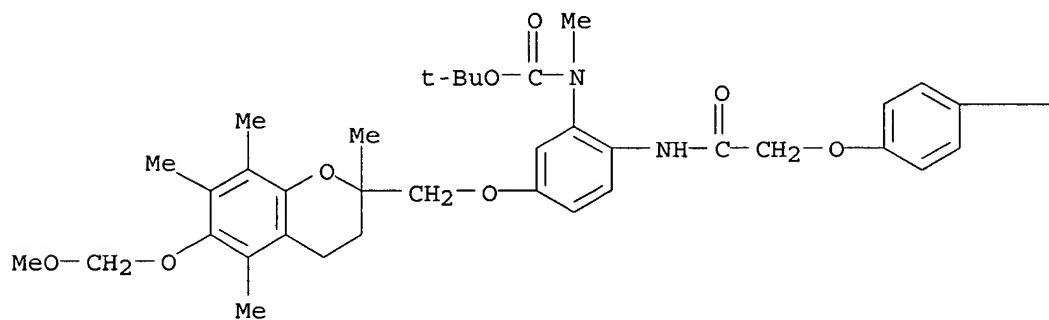


PAGE 1-B



RN 300666-18-6 HCAPLUS  
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PAGE 1-A



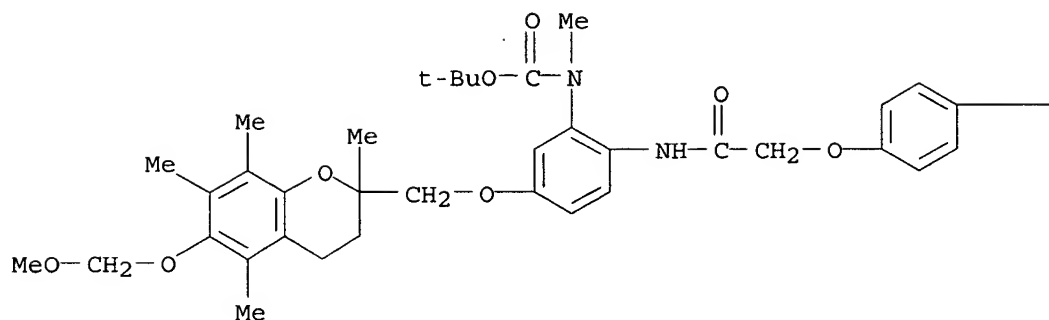
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CN Benzenepropanoic acid, 4-[2-[[4-[[3,4-dihydro-6-(methoxymethoxy)-2,5,7,8-tetramethyl-2H-1-benzopyran-2-yl]methoxy]-2-[[[(1,1-dimethylethoxy)carbonyl]methylamino]phenyl]amino]-2-oxoethoxy]- $\alpha$ -[[4-(1,1-dimethylethyl)phenyl]thio]-, ethyl ester (9CI)  
(CA INDEX NAME)

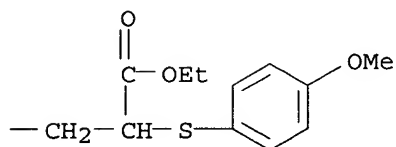
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CN Benzenepropanoic acid, 4-[2-[[[4-[[3,4-dihydro-6-(methoxymethoxy)-2,5,7,8-tetramethyl-2H-1-benzopyran-2-yl]methoxy]-2-[[[(1,1-dimethylethoxy)carbonyl]methylamino]phenyl]amino]-2-oxoethoxy]- $\alpha$ -[[(4-methoxyphenyl)thio]-, ethyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



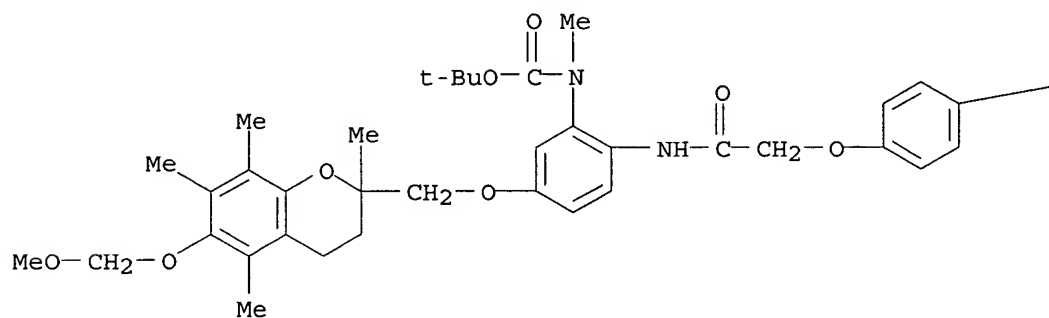
PAGE 1-B



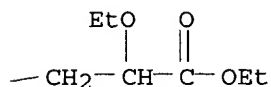
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PAGE 1-A



PAGE 1-B

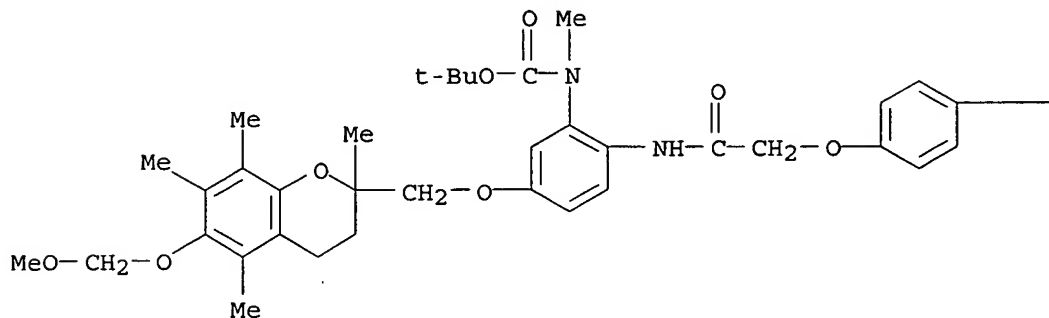


RN 300666-22-2 HCAPLUS

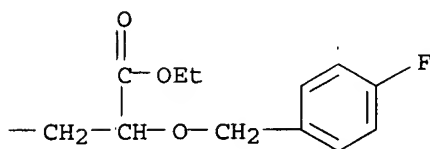
CN Benzenepropanoic acid, 4-[2-[[4-[[3,4-dihydro-6-(methoxymethoxy)-2,5,7,8-tetramethyl-2H-1-benzopyran-2-yl]methoxy]-2-[[1,1-

dimethylethoxy)carbonyl]methylamino]phenyl]amino]-2-oxoethoxy]-  
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 NAME)

PAGE 1-A

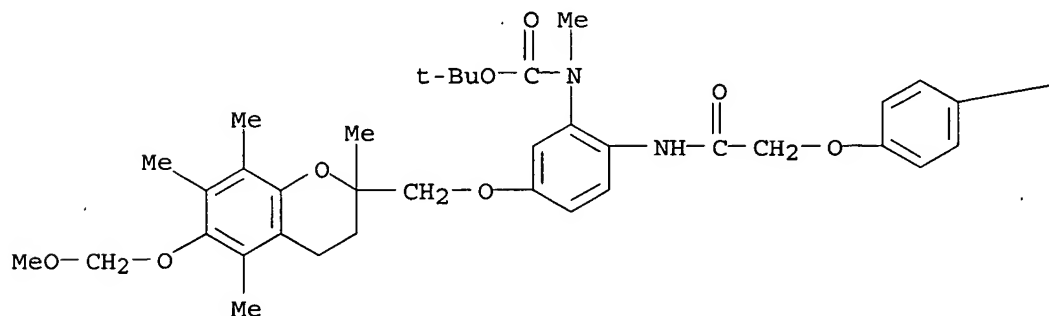


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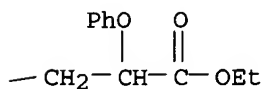


RN 300666-27-7 HCAPLUS  
 CN Benzenepropanoic acid, 4-[2-[[4-[[3,4-dihydro-6-(methoxymethoxy)-  
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 $\alpha$ -phenoxy-, ethyl ester (9CI) (CA INDEX NAME)

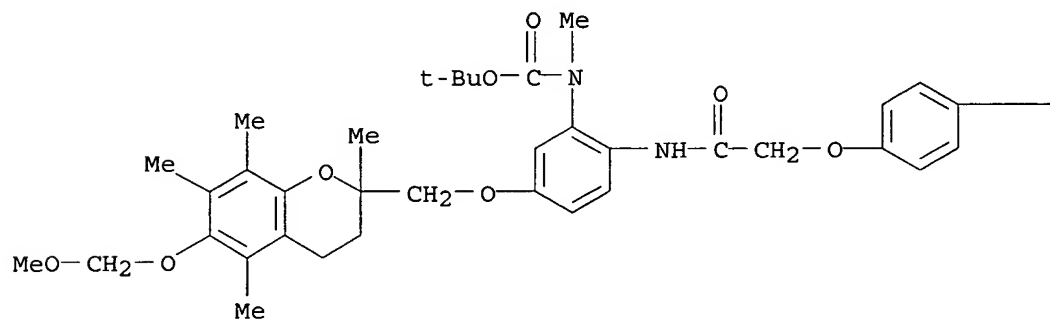
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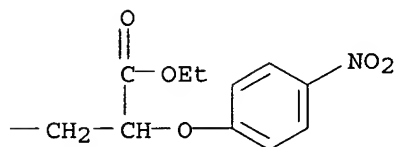
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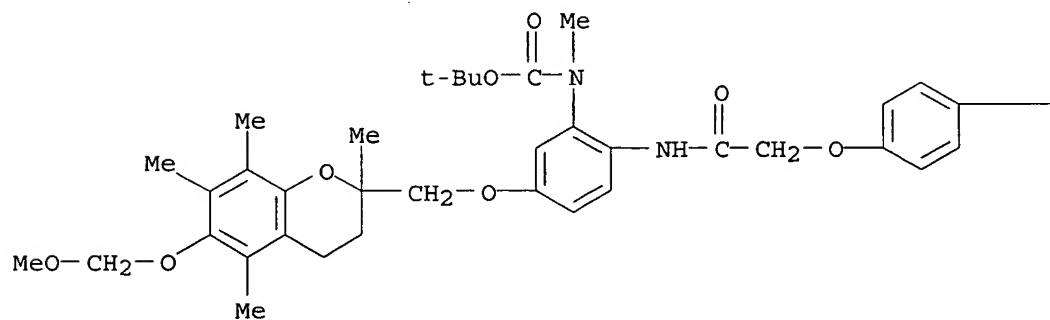
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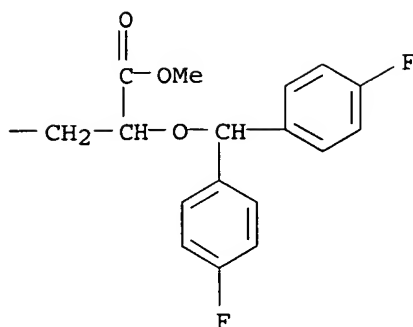
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PAGE 1-A



PAGE 1-B



- IC ICM C07D417-14  
ICS C07D413-14; C07D405-12; C07D471-04; A61K031-427; A61K031-422;  
A61K031-4184; A61K031-437; A61P003-10; A61P029-00;  
A61P037-02; A61P043-00; A61P003-06; A61P003-04; A61P009-12;  
A61P009-10; A61P015-00; A61P009-00
- CC 28-10 (Heterocyclic Compounds (More Than One Hetero Atom))  
Section cross-reference(s): 1, 7
- IT **Peroxisome proliferator-activated receptors**  
(activators; preparation of substituted fused imidazole derivs. as  
therapeutics)
- IT **Diabetes mellitus**  
(complications; preparation of substituted fused imidazole derivs.  
as therapeutics)
- IT Pregnancy  
Pregnancy  
(gestational **diabetes mellitus**; preparation of substituted  
fused imidazole derivs. as therapeutics)
- IT **Diabetes mellitus**  
**Diabetes mellitus**  
(gestational; preparation of substituted fused imidazole derivs. as  
therapeutics)
- IT Allergy inhibitors  
Anti-inflammatory agents  
Antiartherosclerotics  
Antiarthritics  
Antiasthmatics  
**Antidiabetic agents**  
Antihypertensives  
Antiobesity agents  
Antitumor agents  
Antiulcer agents  
Autoimmune disease  
Cachexia  
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Gout  
Hypolipemic agents  
Immunomodulators  
Osteoarthritis  
Osteoporosis  
(preparation of substituted fused imidazole derivs. as therapeutics)
- IT 62517-34-4P 300666-00-6P 300666-01-7P 300666-02-8P  
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(preparation of substituted fused imidazole derivs. as therapeutics)

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE  
 FOR THIS RECORD. ALL CITATIONS AVAILABLE  
 IN THE RE FORMAT

L32 ANSWER 27 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:725618 HCAPLUS

DOCUMENT NUMBER: 133:281783

TITLE: Preparation of benzimidazolylalkoxyphenylalkan  
 oic acid derivatives for the treatment of  
**diabetes** and other diseases

INVENTOR(S): Fujita, Takashi; Wada, Kunio; Oguchi, Minoru;  
 Honma, Hidehito; Fujiwara, Toshihiko;  
 Iwabuchi, Haruo

PATENT ASSIGNEE(S): Sankyo Company, Ltd., Japan

SOURCE: PCT Int. Appl., 235 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000059889	A1	20001012	WO 2000-JP2215	2000 0406

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RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
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BR 2000009593	A	20020618	BR 2000-9593	
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US 2003069294                A1        20030410        US 2001-972206

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US 2004002512                A1        20040101        US 2003-376942

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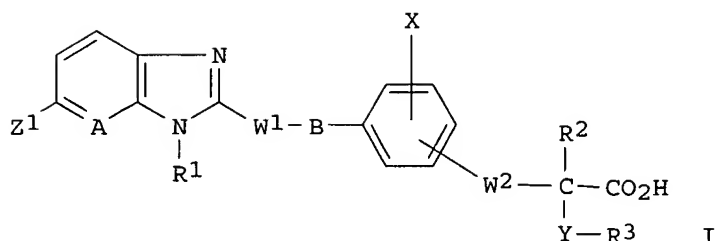
JP 1999-215141               A  
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WO 2000-JP2215               W  
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US 2001-972206               A3  
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OTHER SOURCE(S):  
GI

MARPAT 133:281783



AB The title compds. I [R1 is alkyl or the like; R2 is hydrogen or the like; R3 is hydrogen or the like; A is CH or the like; B is oxygen or the like; W1 is C1-C8 alkylene; W2 is a single bond or C1-C8 alkylene; X is hydrogen or the like; Y is oxygen or the like; and Z1 is alkoxy or the like] are prepared. Feed containing 0.01% 3-[4-[6-(3,5-di-tert-butyl-4-hydroxyphenylthio)-1-methyl-1H-benzimidazol-2-ylmethoxy]phenyl]-2-(4-fluorobenzoyloxy)propionic acid decreased blood sugar in **diabetic** mice by 40.8%. Formulations are given.

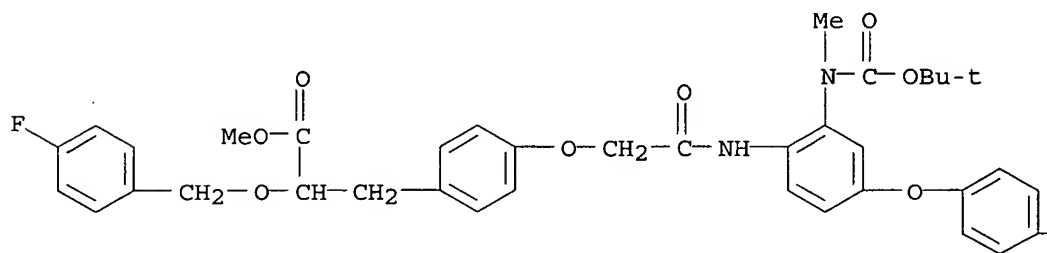
IT 299175-84-1P 299175-86-3P 299175-96-5P  
299176-05-9P

(preparation of benzimidazolylalkoxyphenylalkanoic acid derivs. for treatment of **diabetes** and other diseases)

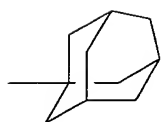
RN 299175-84-1 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[2-[[[(1,1-dimethylethoxy)carbonyl]methylamino]-4-(4-tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylphenoxy)phenyl]amino]-2-oxoethoxy]-α-[(4-fluorophenyl)methoxy]-, methyl ester (9CI) (CA INDEX NAME)

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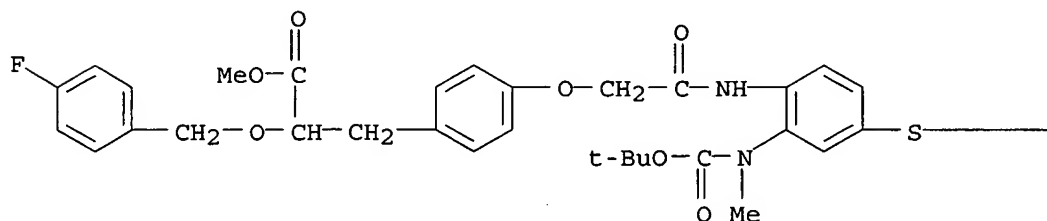
PAGE 1-B



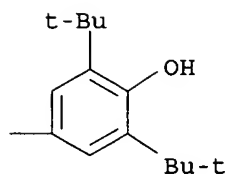
RN 299175-86-3 HCAPLUS

CN Benzenepropanoic acid, 4-[2-[[4-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]thio]-2-[[[(1,1-dimethylethoxy)carbonyl]methylamino]phenyl]amino]-2-oxoethoxy]- $\alpha$ -(4-fluorophenyl)methoxy]-, methyl ester (9CI) (CA INDEX NAME)

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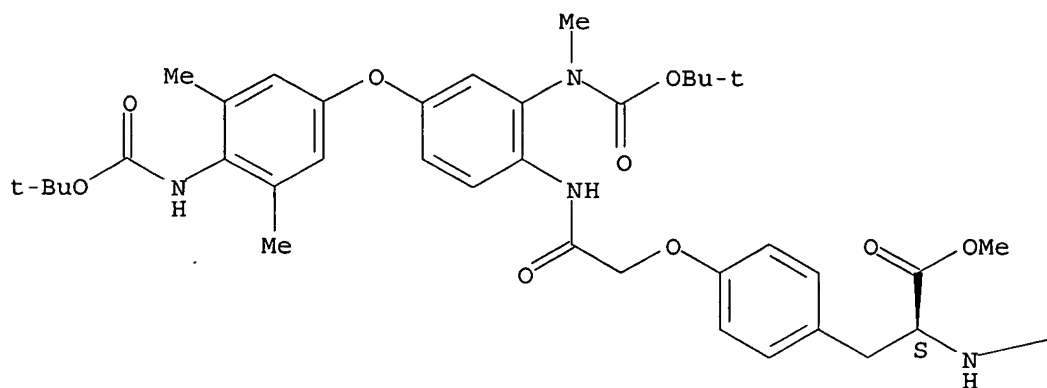


RN 299175-96-5 HCAPLUS

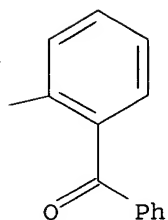
CN L-Tyrosine, N-(2-benzoylphenyl)-O-[2-[[4-[4-[[[(1,1-dimethylethoxy)carbonyl]amino]-3,5-dimethylphenoxy]-2-[[[(1,1-dimethylethoxy)carbonyl]methylamino]phenyl]amino]-2-oxoethyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

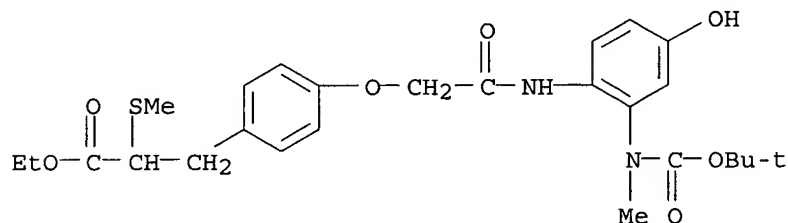
PAGE 1-A



PAGE 1-B



RN 299176-05-9 HCAPLUS  
 CN Benzenepropanoic acid, 4-[2-[[2-[[[(1,1-dimethylethoxy)carbonyl]methylamino]-4-hydroxyphenyl]amino]-2-oxoethoxy]- $\alpha$ -(methylthio)-, ethyl ester (9CI) (CA INDEX NAME)



IC ICM C07D235-16  
 ICS C07H017-02; C07D471-04; C07D401-12; A61K031-4184;  
 A61K031-7056; A61K031-437; A61K031-4439; A61P043-00;  
 A61P003-10; A61P025-00; A61P027-12; A61P009-10; A61P003-06;  
 A61P009-12; A61P029-00; A61P011-06; A61P035-00  
 CC 28-9 (Heterocyclic Compounds (More Than One Hetero Atom))  
 Section cross-reference(s): 1, 63  
 ST benzimidazolylalkoxyphenylalkanoate prepn **antidiabetic**;  
**antidiabetic** benzimidazolylalkoxyphenylalkanoate prepn;  
 disease treatment benzimidazolylalkoxyphenylalkanoate prepn  
 IT Allergy inhibitors  
 Anti-inflammatory agents  
 Antiasthmatics  
**Antidiabetic** agents  
 Antihypertensives  
 Antitumor agents  
 Antiulcer agents  
 Hypolipemic agents  
 Immunomodulators  
 (benzimidazolylalkoxyphenylalkanoic acid derivs.)  
 IT **Diabetes** mellitus  
 (complications; preparation and effect of

- benzimidazolylalkoxyphenylalkanoic acid derivs.)
- IT Pregnancy  
(diabetes; preparation and effect of  
benzimidazolylalkoxyphenylalkanoic acid derivs.)
- IT Kidney, disease  
(diabetic nephropathy; preparation and effect of  
benzimidazolylalkoxyphenylalkanoic acid derivs.)
- IT Cardiovascular system  
(disease, diabetic; preparation and effect of  
benzimidazolylalkoxyphenylalkanoic acid derivs.)
- IT Nerve, disease  
(neuropathy, diabetes related; preparation and effect of  
benzimidazolylalkoxyphenylalkanoic acid derivs.)
- IT Peroxisome proliferator-activated receptors  
(preparation of benzimidazolylalkoxyphenylalkanoic acid derivs. with  
effect on peroxisome proliferator-activated  
receptors)
- IT 299176-23-1P  
(preparation of benzimidazolylalkoxyphenylalkanoic acid derivs. for  
treatment of diabetes and other diseases)
- IT 299175-35-2P  
(preparation of benzimidazolylalkoxyphenylalkanoic acid derivs. for  
treatment of diabetes and other diseases)
- IT 299175-36-3P 299175-37-4P 299175-39-6P 299175-40-9P  
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299176-30-0P  
(preparation of benzimidazolylalkoxyphenylalkanoic acid derivs. for  
treatment of diabetes and other diseases)
- IT 67-64-1, Acetone, reactions 74-88-4, Methyl iodide, reactions  
100-51-6, Benzenemethanol, reactions 107-30-2, Methoxymethyl  
chloride 108-24-7, Acetic anhydride 306-23-0 459-46-1,  
4-Fluorobenzyl bromide 950-59-4 1548-13-6,  
4-Trifluoromethylphenylisocyanate 3096-70-6,  
4-Amino-3,5-dimethylphenol 3580-38-9, 2-Benzoylcyclohexanone  
5188-07-8, Sodium thiomethoxide 5292-43-3, tert-Butyl  
bromoacetate 5437-45-6, Benzyl bromoacetate 7143-01-3,  
Methanesulfonic anhydride 24424-99-5, Di-tert-butyl dicarbonate  
26386-88-9, Diphenylazidophosphate 29799-07-3,  
4-(1-Adamantyl)phenol 51095-47-7, Methyl 4-hydroxyphenyllactate  
68697-61-0, Tyrosine methyl ester hydrochloride 112109-69-0  
150556-70-0, 5-(4-Acetoxybenzyl)thiazolidine-2,4-dione  
179087-93-5 299176-08-2 299176-09-3 299176-10-6  
299176-11-7 299176-13-9 299176-14-0 299176-17-3  
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(preparation of benzimidazolylalkoxyphenylalkanoic acid derivs. for  
treatment of diabetes and other diseases)
- IT 196810-09-0P 197299-03-9P 223133-10-6P 223133-16-2P  
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(preparation of benzimidazolylalkoxyphenylalkanoic acid derivs. for treatment of **diabetes** and other diseases)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE  
 FOR THIS RECORD. ALL CITATIONS AVAILABLE  
 IN THE RE FORMAT

L32 ANSWER 28 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:53564 HCAPLUS

DOCUMENT NUMBER: 132:107781

TITLE: Preparation of phenoxyacetic acid derivatives  
 as selective stimulants of  $\beta$ 3-adrenergic  
 receptor and medicinal compositions containing  
 the same

INVENTOR(S): Tanaka, Nobuyuki; Tamai, Tetsuro; Mukaiyama,  
 Harunobu; Hirabayashi, Akihito; Muranaka,  
 Hideyuki; Sato, Masaaki; Akahanae, Masuo

PATENT ASSIGNEE(S): Kissei Pharmaceutical Co., Ltd., Japan

SOURCE: PCT Int. Appl., 76 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000002846	A1	20000120	WO 1999-JP3611	1999 0705

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W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN,  
 CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,  
 ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT,  
 LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU,  
 SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ,  
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RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY,  
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE,  
 BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2336853	AA	20000120	CA 1999-2336853	1999 0705
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AU 771200	B2	20040318		
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EP 1095932	A1	20010502	EP 1999-926928	1999
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LT 5282 B 20051025 LT 2005-19

2005  
 0228

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PRIORITY APPLN. INFO.: JP 1998-228501

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1998  
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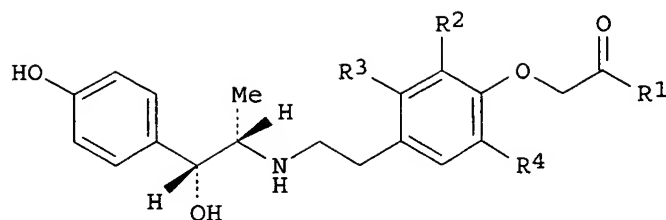
WO 1999-JP3611

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 0705

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OTHER SOURCE(S): MARPAT 132:107781  
 GI



I

AB Novel 4-[2-(((1S,2R)-2-(4-hydroxyphenyl)-2-hydroxy-2-methylethyl)amino)ethyl]phenoxyacetic acid derivs. represented by general formula [I; wherein R1 is hydroxyl, lower alkoxy, aralkoxy, NH2, mono- or di(lower alkyl)amino; one of R2 and R3 is hydrogen, halogeno, lower alkyl, or lower alkoxy, and the other thereof is hydrogen; and R4 is halogeno, lower alkyl, lower haloalkyl, OH, lower alkoxy, aralkoxy, cyano, NO2, NH2, mono- or di(lower alkyl) amino, CONH2, mono- or di(lower alkyl)carbamoyl, NH2, or alkanoylamino] and pharmacol. acceptable salts thereof are prepared These compds. exhibit more potent stimulating effect for  $\beta_3$ -adrenergic receptor than that for  $\beta_1$  and/or  $\beta_2$ -adrenergic receptor and are reduced in side effects due to the stimulating effect for  $\beta_1$  and/or  $\beta_2$ -adrenergic receptor. They are useful as preventive or therapeutic agents for obesity, hyperglycemia, diseases due to hyperkinesia of intestine, pollakiuria, urinary incontinence, depression, cholelithiasis or diseases due to hyperkinesia of biliary tract. Thus, a suspension of 475 mg (1R,2R)-2-amino-1-(4-hydroxyphenyl)propan-1-ol, 520 mg Et 2-[2-bromo-4-(2-bromoethyl)phenoxy]acetate, and 1.42 g mol. sieve 4A in 4.7 mL DMF was stirred at room temperature for 2 days to give, after purification by medium pressure liquid chromatog. using aminopropylated silica gel, 356 mg I (R2 = Br, R3 = R4 = H, R1 = OEt). I.HCl (R1 = OEt, R2 = H, R3 = R4 = Cl) in vitro showed ED50 of  $7.2 \pm 10^{-10}$ ,  $6.8 \pm 10^{-5}$ , and  $6.1 \pm 10^{-6}$  M for stimulating  $\beta_3$ -,  $\beta_1$ -, and  $\beta_2$ -adrenergic receptors in male ferret bladder, atrium of rat heart, and rat uterus, resp.

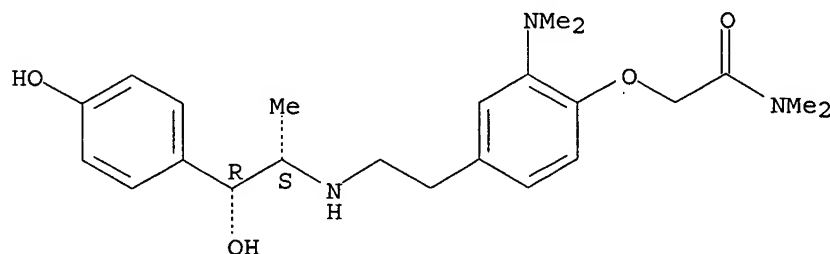
IT 255733-87-0P

(preparation of phenoxyacetic acid derivs. as selective stimulants of  $\beta_3$ -adrenergic receptor for treatment of diseases)

RN 255733-87-0 HCAPLUS

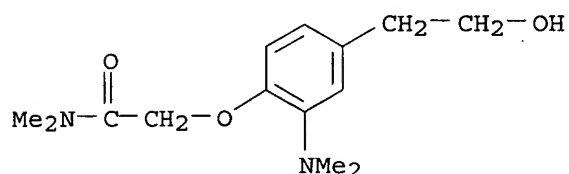
CN Acetamide, 2-[2-(dimethylamino)-4-[2-[[1-(4-hydroxyphenyl)-1-methylethyl]amino]ethyl]phenoxy]-N,N-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

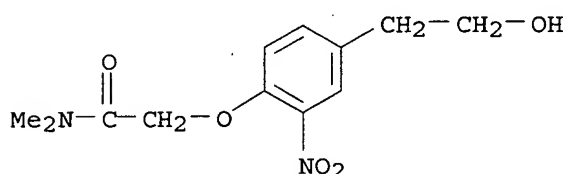




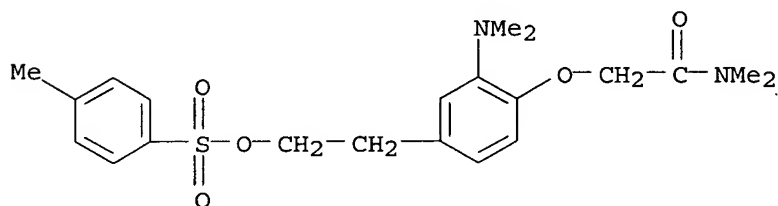
IT 255734-82-8P, 2-[2-(Dimethylamino)-4-(2-hydroxyethyl)phenoxy]-N,N-dimethylacetamide 255734-83-9P  
 , 2-[4-(2-Hydroxyethyl)-2-nitrophenoxy]-N,N-dimethylacetamide 255734-85-1P  
 (preparation of phenoxyacetic acid derivs. as selective stimulants of  $\beta$ 3-adrenergic receptor for treatment of diseases)  
 RN 255734-82-8 HCAPLUS  
 CN Acetamide, 2-[2-(dimethylamino)-4-(2-hydroxyethyl)phenoxy]-N,N-dimethyl- (9CI) (CA INDEX NAME)



RN 255734-83-9 HCAPLUS  
 CN Acetamide, 2-[4-(2-hydroxyethyl)-2-nitrophenoxy]-N,N-dimethyl- (9CI) (CA INDEX NAME)



RN 255734-85-1 HCAPLUS  
 CN Acetamide, 2-[2-(dimethylamino)-4-[2-[(4-methylphenyl)sulfonyl]oxy]ethyl]phenoxy]-N,N-dimethyl- (9CI) (CA INDEX NAME)



IC ICM C07C217-60  
 ICS C07C255-59; C07C235-60; C07C233-43; C07C235-06; A61K031-215; A61K031-195  
 CC 25-19 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)  
 Section cross-reference(s): 1  
 IT Antidepressants  
 Antidiabetic agents  
 Antiobesity agents  
 Calculi, biliary  
 (preparation of phenoxyacetic acid derivs. as selective stimulants of  $\beta$ 3-adrenergic receptor for treatment of diseases)  
 IT 255733-69-8P 255733-70-1P 255733-72-3P 255733-73-4P

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 255734-19-1P

(preparation of phenoxyacetic acid derivs. as selective stimulants  
 of  $\beta_3$ -adrenergic receptor for treatment of diseases)

IT 21092-94-4P, 4'-(Benzyloxy)-3'-hydroxyacetophenone 29121-25-3P,  
 2-(3-Bromo-4-hydroxyphenyl)acetic acid ethyl ester 39624-10-7P  
 50824-04-9P, 4-Bromo-2-(trifluoromethyl)phenol 110925-45-6P  
 118172-64-8P 169247-46-5P, Benzyl 4-bromo-2-  
 (trifluoromethyl)phenyl ether 191165-12-5P 201662-73-9P,  
 2-(Benzyloxy)-5-vinylbenzoic acid 222843-69-8P 234757-51-8P,  
 2-(4-(Benzyloxy)-3-bromophenyl)acetic acid ethyl ester  
 252563-24-9P 255734-20-4P, 2-[2-Bromo-4-(2-  
 bromoacetyl)phenoxy]acetic acid ethyl ester 255734-21-5P,  
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 255734-22-6P, 2-[4-(2-Bromoacetyl)-2,5-dimethylphenoxy]acetic acid  
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 2-[4-(2-Bromoacetyl)-2-chloro-5-methylphenoxy]acetic acid ethyl  
 ester 255734-25-9P, 2-[4-(2-Bromoacetyl)-2,5-  
 difluorophenoxy]acetic acid ethyl ester 255734-26-0P,  
 2-[4-(2-Bromoacetyl)-2-hydroxyphenoxy]acetic acid ethyl ester  
 255734-27-1P, 4'-(Benzyloxy)-3'-(methoxymethoxy)acetophenone  
 255734-28-2P, 2-[4-Acetyl-2-(methoxymethoxy)phenoxy]acetic acid  
 ethyl ester 255734-29-3P, 2-[4-(2-Bromoacetyl)-2-  
 ethoxyphenoxy]acetic acid ethyl ester 255734-30-6P,  
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 255734-31-7P, 2-[4-(2-Bromoethyl)-2-ethylphenoxy]acetic acid ethyl  
 ester 255734-32-8P, 2-[4-(2-Bromoethyl)-2-ethoxyphenoxy]acetic  
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 dichlorophenol 255734-41-9P, 4-(2-Bromoethyl)-2-fluorophenol  
 255734-42-0P 255734-43-1P 255734-44-2P 255734-45-3P,  
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 255734-50-0P 255734-51-1P, 2-[4-(2-Hydroxyethyl)-2-  
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2-[4-(2-Bromoethyl)-2-(trifluoromethyl)phenoxy]acetic acid ethyl  
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2-[4-(2-Bromoethyl)-2-cyanophenoxy]acetic acid ethyl ester  
255734-69-1P, 2-[4-(2-Bromoethyl)-5-chloro-2-methoxyphenoxy]acetic  
acid ethyl ester 255734-70-4P, 2-[4-(2-Bromoethyl)-5-chloro-2-  
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2-[4-(2-Bromoethyl)-2-chloro-5-methoxyphenoxy]acetic acid ethyl  
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2-(Benzyloxy)-5-formylbenzoic acid methyl ester 255734-74-8P,  
2-(Benzyloxy)-5-vinylbenzoic acid methyl ester 255734-75-9P,  
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, 2-[4-(2-Hydroxyethyl)-2-nitrophenoxy]-N,N-dimethylacetamide  
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255734-93-1P, 2-[2-Bromo-4-(2-bromoethyl)phenoxy]acetic acid ethyl  
ester

(preparation of phenoxyacetic acid derivs. as selective stimulants  
of  $\beta_3$ -adrenergic receptor for treatment of diseases)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE  
FOR THIS RECORD. ALL CITATIONS AVAILABLE  
IN THE RE FORMAT

L32 ANSWER 29 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:184222 HCAPLUS

DOCUMENT NUMBER: 130:223585

TITLE: Preparation of substituted phenylalanine  
derivatives as protein tyrosine phosphatase  
inhibitors

INVENTOR(S): Larsen, Scott D.; May, Paul D.; Bleasdale,  
John; Liljebris, Charlotta; Schostarez,  
Heinrich Josef; Barf, Tjeerd

PATENT ASSIGNEE(S): Pharmacia & Upjohn Company, USA

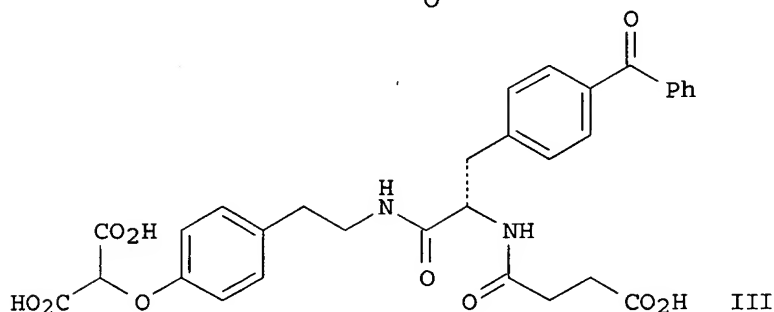
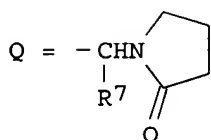
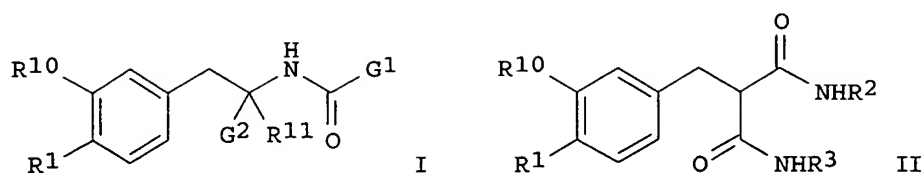
SOURCE: PCT Int. Appl., 182 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 3  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9911606	A2	19990311	WO 1998-US17327	1998 0824
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WO 9911606	A3	19990708		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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EP 1019364	A2	20000719	EP 1998-944476	1998 0824
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JP 2001514245	T2	20010911	JP 2000-508647	1998 0824
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AT 268750	E	20040615	AT 1998-944476	1998 0824
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PRIORITY APPLN. INFO.:			US 1997-57730P	P 1997 0828
<--				
			WO 1998-US17327	W 1998 0824
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OTHER SOURCE(S):	MARPAT 130:223585			
GI				



AB The present invention comprises title compds. I and II [G1 = R2, NR8R4; G2 = H, CONHR3, CH2OH, CH:CHR3; R1 = OSO3H, OCH(CO2R5)2, OCH2CO2R5, OCH(CO2R5)CH2CO2R5, O(CO2R5):CHCO2R5, CH2CH(CO2R5)2, CH:C(CO2R5)2, OCH2CONHOH, N(CH2CO2R5)2, OCHFCO2R5; R2 = C1-10 alkyl, C3-8 cycloalkyl, C0-6 alkylphenyl each substituted with 0-2 CO2R5 groups or 0-1 CONH2 groups, CHR7NHXR6, group Q; R3 = (un)substituted C1-12 alkyl, C1-4 alkyl-C3-6 cycloalkyl, C2-12 alkenyl, C3-12 alkynyl, (un)substituted C0-10 alkyl(G3)n, CH(CONH2)-C1-12 alkyl; R4 = H, C1-18 alkyl, alkenyl, C0-6 alkyl-G3; R5 = H, C1-10 alkyl, C1-5 alkylphenyl; R6 = C1-10 alkyl, substituted C1-6 alkyl; R7 = H, substituted C1-6 alkyl; R8 = C0-6 alkyl-G3, CHR7CO2R5, CHR7CH2CO2R5, CHR7CONHCH2COR5; G3 = (un)substituted Ph, naphthyl, heterocyclyl; R10 = H, CO2R5, CONHOH, 5-tetrazolyl, F, OCH2CO2R5; R11 = H, Me; X = CO, SO2, CO2; n = 0-3; with provisos] and pharmaceutically acceptable salts thereof, as small mol. weight, non-peptidic inhibitors of protein tyrosine phosphatase 1 (PTP1) which are useful for the treatment and/or prevention of non-insulin dependent **diabetes mellitus** (NIDDM). Thus, O-alkylation of N-tert-butoxycarbonyltyramine with di-Et chloromalonate, followed by acidic deprotection, amidation with 4-benzoyl-N-tert-butoxycarbonyl-L-phenylalanine, acidic deprotection, and amidation with succinic anhydride, gave desired title compound III (PNU 176073). III showed 60% inhibition of protein tyrosine phosphatase 1B at a concentration of 10  $\mu$ M.

IT 221076-84-2P

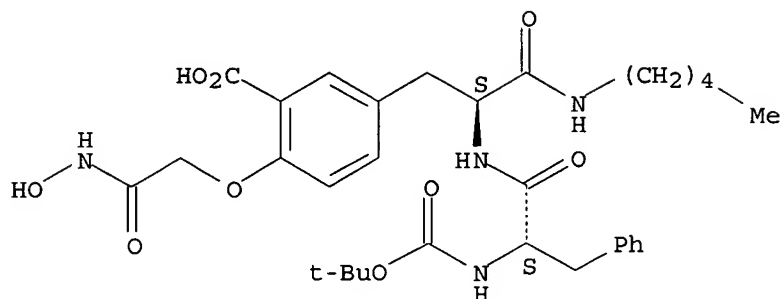
(preparation of substituted phenylalanine derivs. as protein tyrosine phosphatase inhibitors)

RN 221076-84-2 HCAPLUS

CN L-Tyrosinamide, N-[(1,1-dimethylethoxy)carbonyl]-L-phenylalanyl-3-carboxy-O-[2-(hydroxyamino)-2-oxoethyl]-N-pentyl- (9CI) (CA INDEX

NAME)

Absolute stereochemistry.



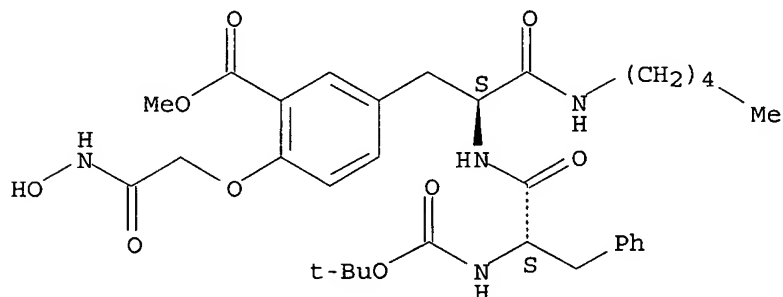
IT 221077-60-7P

(preparation of substituted phenylalanine derivs. as protein tyrosine phosphatase inhibitors)

RN 221077-60-7 HCAPLUS

CN L-Tyrosinamide, N-[(1,1-dimethylethoxy)carbonyl]-L-phenylalanyl-O-[2-(hydroxyamino)-2-oxoethyl]-3-(methoxycarbonyl)-N-pentyl- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.



IC ICM C07C235-00

CC 34-3 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 1, 7, 63

ST phenylalanine deriv prepn protein tyrosine phosphatase inhibitor;  
noninsulin dependent **diabetes** mellitus treatment  
phenylalanine deriv prepn

IT **Diabetes** mellitus

(non-insulin-dependent; preparation of substituted phenylalanine derivs. as protein tyrosine phosphatase inhibitors)

IT	221075-08-7P	221075-11-2P	221075-12-3P	221075-13-4P
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	221075-34-9P	221075-36-1P	221075-37-2P	221075-38-3P
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221076-93-3P	221076-94-4P	221076-95-5P	

(preparation of substituted phenylalanine derivs. as protein tyrosine phosphatase inhibitors)

IT 40829-20-7P	40904-59-4P	108376-28-9P	134081-15-5P
141360-76-1P	159560-93-7P	221076-98-8P	221077-00-5P
221077-01-6P	221077-02-7P	221077-03-8P	221077-04-9P
221077-05-0P	221077-07-2P	221077-08-3P	221077-09-4P
221077-10-7P	221077-11-8P	221077-12-9P	221077-13-0P
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221077-45-8P	221077-46-9P	221077-47-0P	221077-48-1P
221077-49-2P	221077-50-5P	221077-51-6P	221077-52-7P
221077-53-8P	221077-54-9P	221077-55-0P	221077-56-1P
221077-57-2P	221077-58-3P	221077-59-4P	221077-60-7P
221077-61-8P	221077-62-9P	221077-63-0P	221077-64-1P
221077-65-2P	221077-66-3P	221077-67-4P	221077-68-5P
221077-69-6P	221077-70-9P	221077-71-0P	221077-72-1P
221077-73-2P	221077-74-3P	221077-75-4P	221077-76-5P
221077-77-6P	221077-78-7P	221077-79-8P	221077-80-1P
221077-81-2P	221077-82-3P	221077-83-4P	221077-86-7P
221077-90-3P	221077-95-8P	221077-97-0P	221077-98-1P
221077-99-2P	221078-02-0P	221078-04-2P	221078-06-4P
221078-08-6P	221078-09-7P	221078-10-0P	

(preparation of substituted phenylalanine derivs. as protein tyrosine phosphatase inhibitors)

L32 ANSWER 30 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:113706 HCAPLUS

DOCUMENT NUMBER: 130:168661

TITLE: Preparation of N-sulfonyl phenylalanine dipeptide derivatives and analogs as inhibitors of leukocyte adhesion mediated by

INVENTOR(S): VLA-4  
 Thorsett, Eugene D.; Semko, Christopher M.;  
 Sarantakis, Dimitrios; Pleiss, Michael A.;  
 Lombardo, Louis John; Kreft, Anthony; Konradi,  
 Andrei W.; Grant, Francine S.; Dressen, Darren  
 B.; Dappen, Michael S.; Baudy, Reinhardt  
 Bernhard; Ashwell, Susan

PATENT ASSIGNEE(S): Athena Neurosciences, Inc., USA; American Home  
 Products Corporation

SOURCE: PCT Int. Appl., 254 pp.  
 CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9906431	A1	19990211	WO 1998-US15313	1998 0730
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2290747	AA	19990211	CA 1998-2290747	1998 0730
AU 9886611	A1	19990222	AU 1998-86611	1998 0730
AU 756696	B2	20030123		
ZA 9806827	A	20000502	ZA 1998-6827	1998 0730
EP 1001972	A1	20000524	EP 1998-937990	1998 0730
BR 9812114	A	20000718	BR 1998-12114	1998 0730
JP 2001512134	T2	20010821	JP 2000-505186	1998 0730
NZ 502582	A	20020726	NZ 1998-502582	



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CN 1133648	B	20040107	CN 1998-807753	
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TW 534910	B	20030601	TW 1998-87112638	
				1998 0731
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NO 2000000450	A	20000328	NO 2000-450	
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			<--	
PRIORITY APPLN. INFO.:			US 1997-920394	A1 1997 0731
			<--	
			WO 1998-US15313	W 1998 0730
			<--	

OTHER SOURCE(S): MARPAT 130:168661

AB Disclosed are title compds. R1SO2NR2CHR3QCHR5COR6 [R1 = (un)substituted alkyl, (un)substituted aryl, (un)substituted cycloalkyl, (un)substituted heterocyclyl; R2 = H, any group R1; R1R2 may form (un)substituted heterocyclic ring; R3 = H, any group R1; R2R3 may form (un)substituted heterocyclic ring; R5 = (CH2)x-Ar-R5'; R5' = substituted alkylcarbonylamino, alkoxyaryl, aryl, heteroaryl, NR2, alkoxy-NR2, alkenyl, alkynyl, aryloxy, heteroaryloxy, tetrazolyl, etc.; each R = H, any group R1; Ar = (un)substituted aryl or heteroaryl; x = 1-4; Q = C(X)NR7; R7 = H, alkyl; X = O, S; R6 = NH2, (un)substituted alkoxy, (un)substituted cycloalkoxy, succinimidyloxy, adamantylamino,  $\beta$ -cholest-5-en-3-yloxy, NHOY, NH(CH2)pCO2Y, OCH2NR9R10; Y = H, (un)substituted alkyl, (un)substituted aryl; p = 1-8; R9 = (un)substituted CO-aryl; R10 = H, CH2CO2R11, NHSO2Z; R11 = alkyl; Z = (un)substituted alkyl, (un)substituted cycloalkyl, (un)substituted aryl, (un)substituted heteroaryl, (un)substituted heterocyclyl; and pharmaceutically acceptable salts thereof, with provisos] which bind VLA-4 (also referred to as integrin  $\alpha 4 \beta 1$  and CD49d/CD29). Certain of these compds. also inhibit leukocyte adhesion and, in particular, leukocyte adhesion mediated by VLA-4.

Such compds. are useful in the treatment of inflammatory diseases in a mammalian patient, e.g., human, wherein the disease may be, for example, asthma, Alzheimer's disease, atherosclerosis, AIDS dementia, **diabetes**, inflammatory bowel disease, rheumatoid arthritis, tissue transplantation, tumor metastasis and myocardial ischemia. The compds. can also be administered for the treatment of inflammatory brain diseases such as multiple sclerosis. Thus, BOP-mediated peptide coupling of Ts-Pro-Phe(4-NH2)-OMe (Ts = tosyl) with Boc-Gly-OH, followed by saponification, gave desired title compound Ts-Pro-Phe(4-Boc-Gly-NH)-OH. All prepared compds. have IC50  $\leq$  15  $\mu$ M in a VLA-4 binding assay.

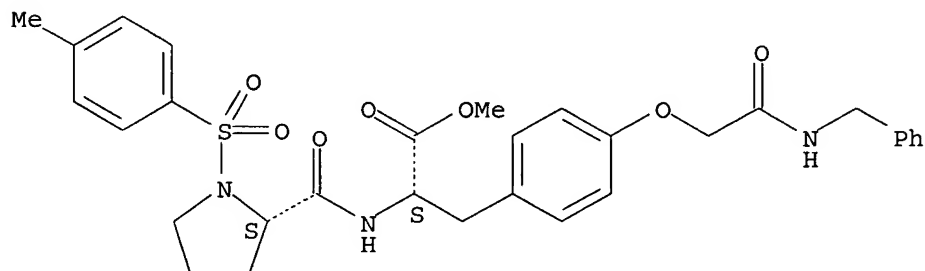
IT 220397-47-7P

(preparation of N-sulfonyl phenylalanine dipeptide derivs. and analogs as inhibitors of leukocyte adhesion mediated by VLA-4)

RN 220397-47-7 HCAPLUS

CN L-Tyrosine, 1-[(4-methylphenyl)sulfonyl]-L-prolyl-O-[2-oxo-2-[(phenylmethyl)amino]ethyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



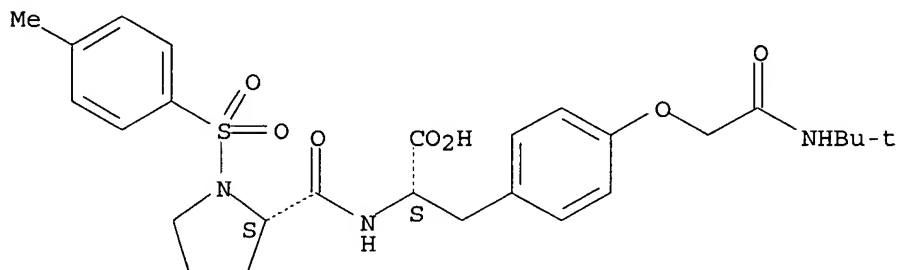
IT 220397-52-4P 220398-16-3P 220398-17-4P

(preparation of N-sulfonyl phenylalanine dipeptide derivs. and analogs as inhibitors of leukocyte adhesion mediated by VLA-4)

RN 220397-52-4 HCAPLUS

CN L-Tyrosine, 1-[(4-methylphenyl)sulfonyl]-L-prolyl-O-[2-[(1,1-dimethylethyl)amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)

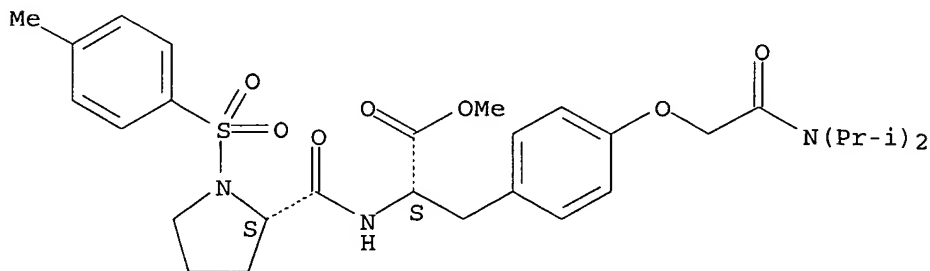
Absolute stereochemistry.



RN 220398-16-3 HCAPLUS

CN L-Tyrosine, 1-[(4-methylphenyl)sulfonyl]-L-prolyl-O-[2-[bis(1-methylethyl)amino]-2-oxoethyl]-, methyl ester (9CI) (CA INDEX NAME)

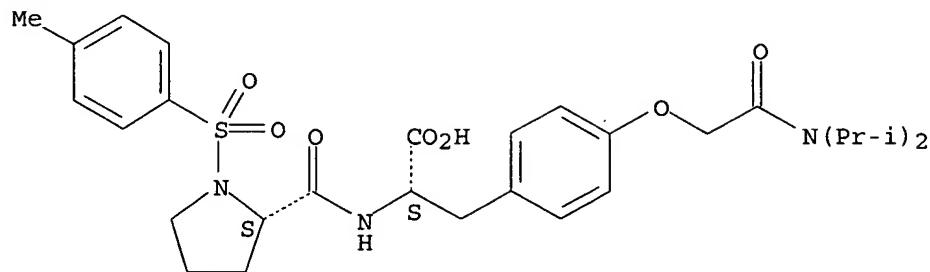
Absolute stereochemistry.



RN 220398-17-4 HCAPLUS

CN L-Tyrosine, 1-[(4-methylphenyl)sulfonyl]-L-prolyl-O-[2-[bis(1-methylethyl)amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IC ICM C07K005-062  
ICS C07K005-065; C07K005-078; A61K038-05  
CC 34-3 (Amino Acids, Peptides, and Proteins)  
Section cross-reference(s): 1, 15, 63  
IT Anti-Alzheimer's agents  
Antiasthmatics  
Antidiabetic agents  
Antirheumatic agents  
Encephalitis  
Meningitis  
Psoriasis  
Transplant and Transplantation  
(preparation of N-sulfonyl phenylalanine dipeptide derivs. and  
analogs as inhibitors of leukocyte adhesion mediated by VLA-4)  
IT 220396-90-7P 220397-05-7P 220397-07-9P 220397-21-7P  
220397-25-1P 220397-42-2P 220397-43-3P 220397-45-5P  
220397-47-7P 220398-14-1P 220398-29-8P  
(preparation of N-sulfonyl phenylalanine dipeptide derivs. and  
analogs as inhibitors of leukocyte adhesion mediated by VLA-4)  
IT 220396-92-9P 220396-93-0P 220396-94-1P 220396-95-2P  
220396-96-3P 220396-97-4P 220396-98-5P 220396-99-6P  
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 220398-31-2P 220398-32-3P 220398-33-4P

(preparation of N-sulfonyl phenylalanine dipeptide derivs. and  
 analogs as inhibitors of leukocyte adhesion mediated by VLA-4)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE  
 FOR THIS RECORD. ALL CITATIONS AVAILABLE  
 IN THE RE FORMAT

L32 ANSWER 31 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:693417 HCAPLUS

DOCUMENT NUMBER: 129:343326

TITLE: Preparation of benzenes as protein kinase C  
 inhibitors

INVENTOR(S): Mori, Toyoki; Tominaga, Michiaki; Tabusa,  
 Fujio; Ei, Kazuyoshi; Nakaya, Kenji; Takemura,  
 Isao; Shinohara, Tomokazu; Tanada, Yoshihisa;  
 Yamauchi, Takahito; Kitano, Kazuyoshi

PATENT ASSIGNEE(S): Otsuka Pharmaceutical Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 359 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

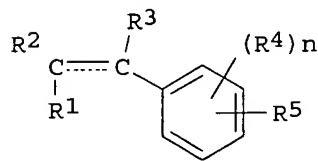
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 10287634	A2	19981027	JP 1997-110527	1997 0411

PRIORITY APPLN. INFO.: <--  
 JP 1997-110527  
 1997  
 0411

OTHER SOURCE(S): MARPAT 129:343326  
 GI



I

AB Benzenes I [R1 = 5- to 6-membered (un)substituted unsatd.  
 heterocyclyl having 1-4 N, O, or S; cyano, carboxylalkyl,  
 alkoxycarbonyl, H, Bz, (un)substituted amido, etc.; R2 =  
 (un)substituted Bz, (un)substituted 1,2,3,4-  
 tetrahydroquinolinylcarbonyl, pyridylcarbonyl, (un)substituted

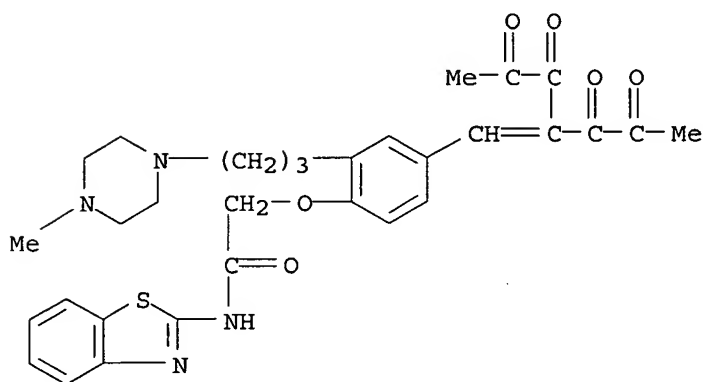
phenoxy carbonyl, etc.; R3 = H, lower alkyl, PhS, (un)substituted lower alkylthio, cycloalkylthio, cyano, etc.; R4 = H, (un)substituted lower alkyl, lower alkoxy, (un)substituted aminoalkylene, (un)substituted aminoalkylenyloxy; R5 = substituted alkenyl, phenylthioureidocarbonyl, pyrimidylaminocarbonylalkoxy, etc.; n = 1-3; the dot line may be double bond] or their salts are prepared. I are useful for prevention and treatment of chronic rheumatoid arthritis, systemic lupus erythematosus, atopic dermatitis, heart failure, allergy, multiple sclerosis, tumor, Alzheimer-type dementia, etc. Condensation of 250 mg 2-(benzoylmethyl)pyridine with 300 mg 4-[(2-benzothiazolyl)aminocarbonyl]benzaldehyde in C6H6 for 10 h gave 0.3 g 2-[4-[2-benzoyl-2-(2-pyridyl)vinyl]benzoylamino]benzothiazole.

IT 215507-40-7P

(preparation of benzenes as protein kinase C inhibitors for treatment of diseases)

RN 215507-40-7 HCAPLUS

CN Acetamide, N-2-benzothiazolyl-2-[4-[2-(1,2-dioxopropyl)-3,4-dioxo-1-pentenyl]-2-[3-(4-methyl-1-piperazinyl)propyl]phenoxy]-, dihydrochloride (9CI) (CA INDEX NAME)



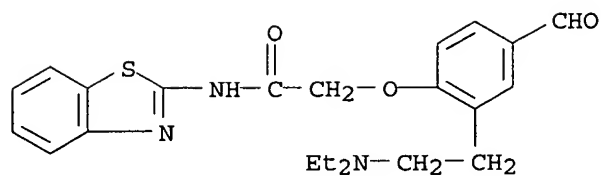
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IT 202991-38-6P 202991-39-7P 202991-40-0P  
 202991-41-1P 202991-44-4P 202991-45-5P  
 202991-46-6P 202991-51-3P 202991-58-0P  
 202991-60-4P 202991-63-7P 202991-66-0P  
 202991-67-1P 202991-68-2P 202994-44-3P  
 215503-91-6P 215504-01-1P 215504-08-8P  
 215504-09-9P

(preparation of benzenes as protein kinase C inhibitors for treatment of diseases)

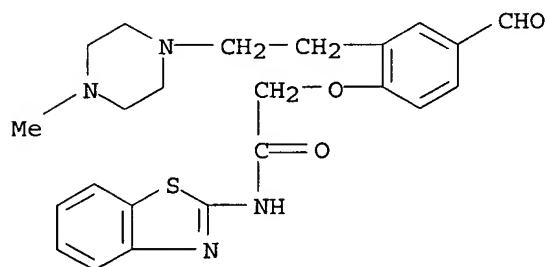
RN 202991-38-6 HCAPLUS

CN Acetamide, N-2-benzothiazolyl-2-[2-[2-(diethylamino)ethyl]-4-formylphenoxy]-, monohydrochloride (9CI) (CA INDEX NAME)



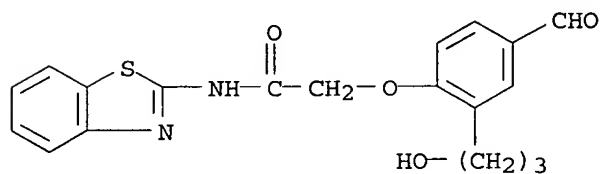
● HCl

RN 202991-39-7 HCAPLUS  
 CN Acetamide, N-2-benzothiazolyl-2-[4-formyl-2-[2-(4-methyl-1-piperazinyl)ethyl]phenoxy]-, dihydrochloride (9CI) (CA INDEX NAME)

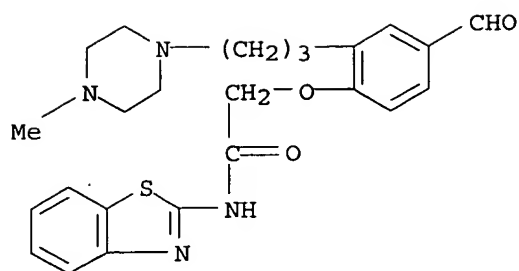


● 2 HCl

RN 202991-40-0 HCAPLUS  
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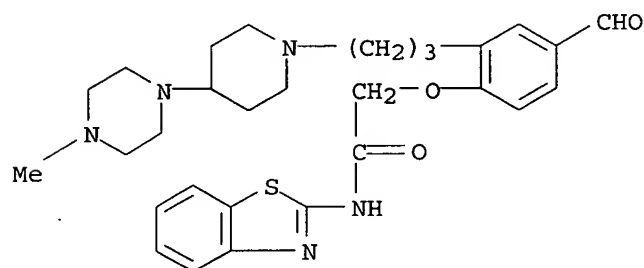


RN 202991-41-1 HCAPLUS  
 CN Acetamide, N-2-benzothiazolyl-2-[4-formyl-2-[3-(4-methyl-1-piperazinyl)propyl]phenoxy]- (9CI) (CA INDEX NAME)



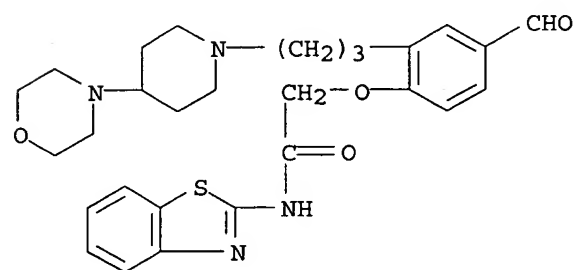
RN 202991-44-4 HCAPLUS

CN Acetamide, N-2-benzothiazolyl-2-[4-formyl-2-[3-[4-(4-methyl-1-piperazinyl)-1-piperidinyl]propyl]phenoxy]- (9CI) (CA INDEX NAME)



RN 202991-45-5 HCAPLUS

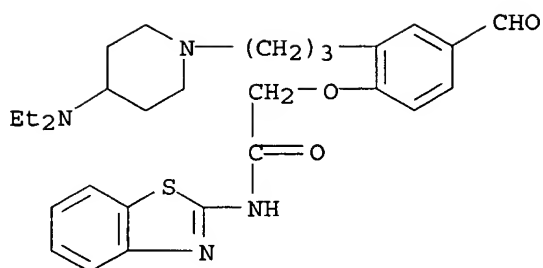
CN Acetamide, N-2-benzothiazolyl-2-[4-formyl-2-[3-[4-(4-morpholinyl)-1-piperidinyl]propyl]phenoxy]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 202991-46-6 HCAPLUS

CN Acetamide, N-2-benzothiazolyl-2-[2-[3-[4-(diethylamino)-1-piperidinyl]propyl]-4-formylphenoxy]-, dihydrochloride (9CI) (CA INDEX NAME)

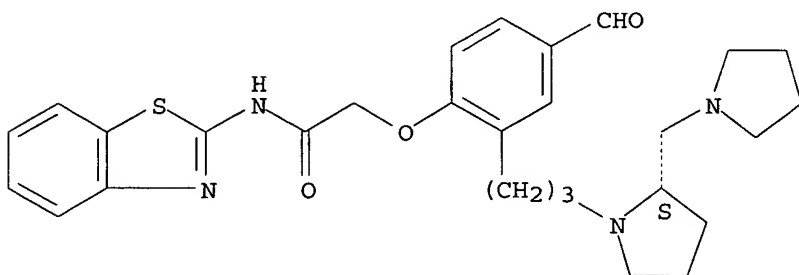


● 2 HCl

RN 202991-51-3 HCAPLUS

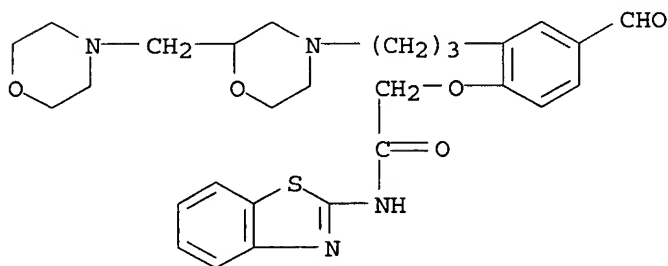
CN Acetamide, N-2-benzothiazolyl-2-[4-formyl-2-[3-[(2S)-2-(1-pyrrolidinylmethyl)-1-pyrrolidinyl]propyl]phenoxy] - (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 202991-58-0 HCAPLUS

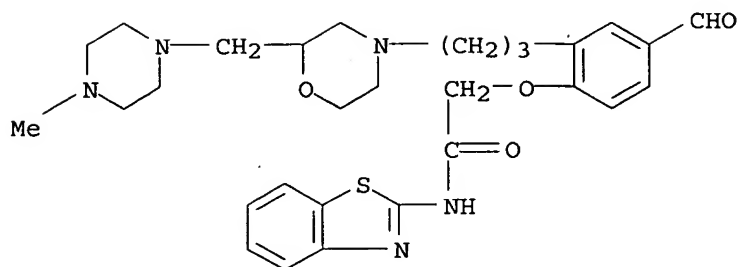
CN Acetamide, N-2-benzothiazolyl-2-[4-formyl-2-[3-[2-(4-morpholinylmethyl)-4-morpholinyl]propyl]phenoxy] - (9CI) (CA INDEX NAME)



RN 202991-60-4 HCAPLUS

CN Acetamide, N-2-benzothiazolyl-2-[4-formyl-2-[3-[2-[(4-methyl-1-piperazinyl)methyl]-4-morpholinyl]propyl]phenoxy] - (9CI) (CA INDEX NAME)

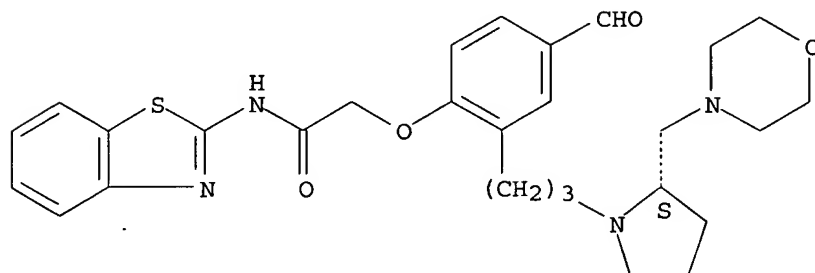




RN 202991-63-7 HCAPLUS

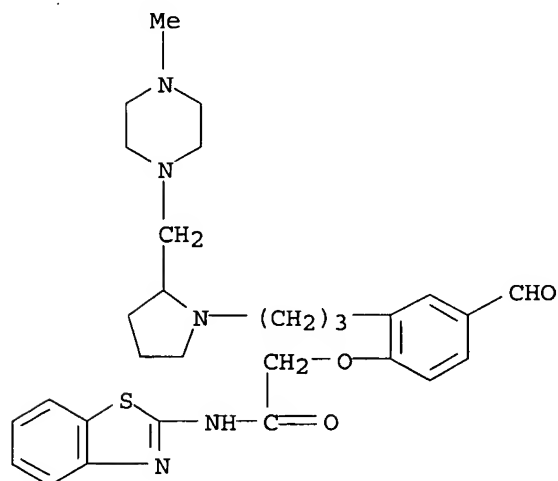
CN Acetamide, N-2-benzothiazolyl-2-[4-formyl-2-[3-[(2S)-2-(4-morpholinylmethyl)-1-pyrrolidinyl]propyl]phenoxy]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



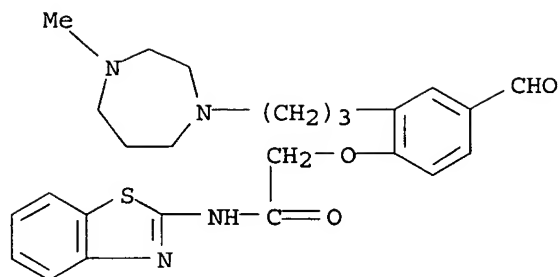
RN 202991-66-0 HCAPLUS

CN Acetamide, N-2-benzothiazolyl-2-[4-formyl-2-[3-[2-[(4-methyl-1-piperazinyl)methyl]-1-pyrrolidinyl]propyl]phenoxy]-(9CI) (CA INDEX NAME)



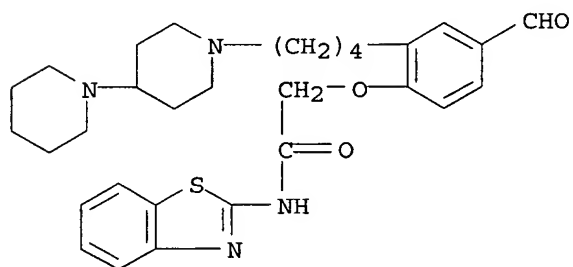
RN 202991-67-1 HCAPLUS

CN Acetamide, N-2-benzothiazolyl-2-[4-formyl-2-[3-(hexahydro-4-methyl-1H-1,4-diazepin-1-yl)propyl]phenoxy]-(9CI) (CA INDEX NAME)



RN 202991-68-2 HCAPLUS

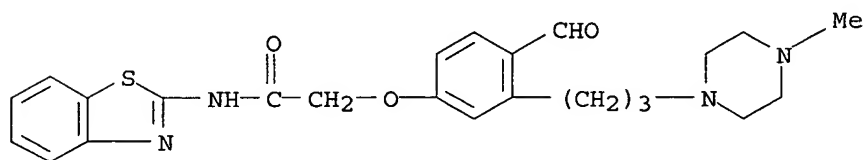
CN Acetamide, N-2-benzothiazolyl-2-[2-(4-[1,4'-bipiperidin]-1'-ylbutyl)-4-formylphenoxy]-, trihydrochloride (9CI) (CA INDEX NAME)



● 3 HCl

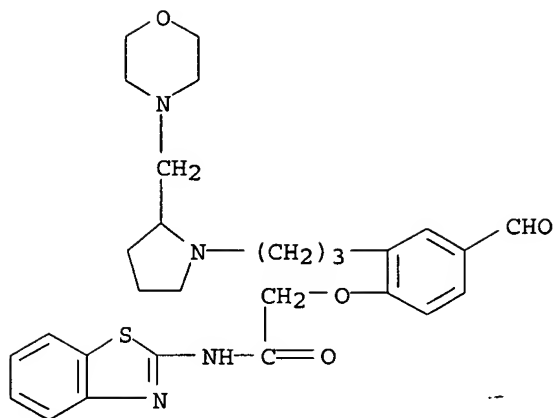
RN 202994-44-3 HCAPLUS

CN Acetamide, N-2-benzothiazolyl-2-[4-formyl-3-[3-(4-methyl-1-piperazinyl)propyl]phenoxy]- (9CI) (CA INDEX NAME)



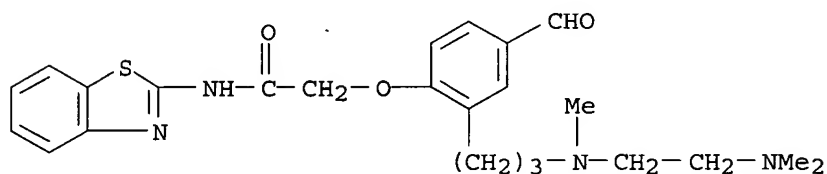
RN 215503-91-6 HCAPLUS

CN Acetamide, N-2-benzothiazolyl-2-[4-formyl-2-[3-[2-(4-morpholinylmethyl)-1-pyrrolidinyl]propyl]phenoxy]- (9CI) (CA INDEX NAME)



RN 215504-01-1 HCAPLUS

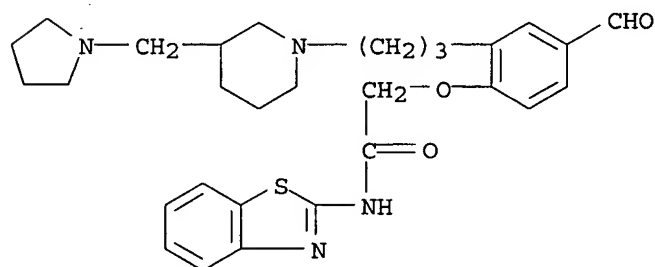
CN Acetamide, N-2-benzothiazolyl-2-[2-[3-[[2-(dimethylamino)ethyl]methylamino]propyl]-4-formylphenoxy]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

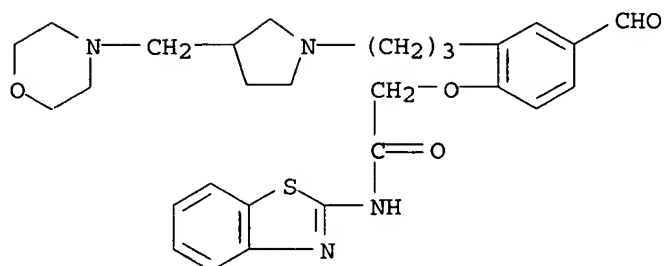
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RN 215504-09-9 HCAPLUS

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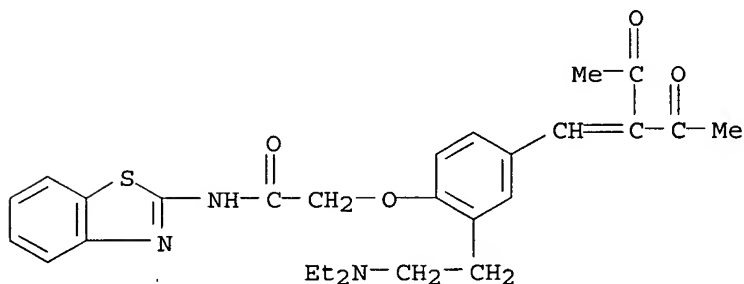


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(preparation of benzenes as protein kinase C inhibitors for treatment of diseases)

RN 215507-34-9 HCAPLUS

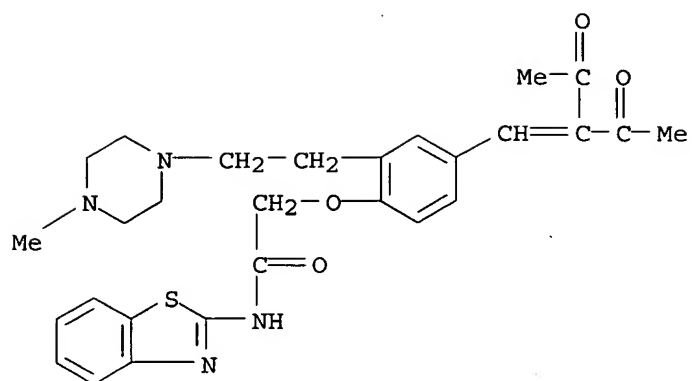
CN Acetamide, 2-[4-(2-acetyl-3-oxo-1-butenyl)-2-[2-(diethylamino)ethyl]phenoxy]-N-2-benzothiazolyl-, monohydrochloride (9CI) (CA INDEX NAME)



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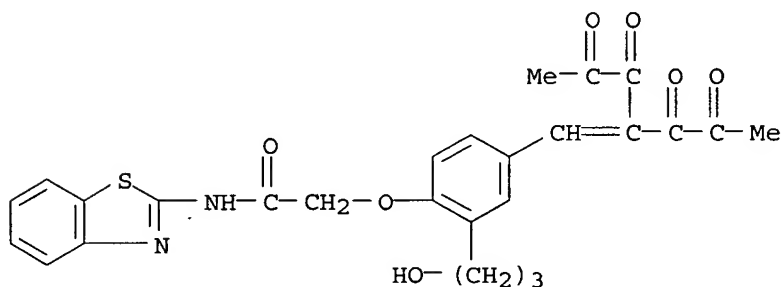
CN Acetamide, 2-[4-(2-acetyl-3-oxo-1-butenyl)-2-[2-(4-methyl-1-piperazinyl)ethyl]phenoxy]-N-2-benzothiazolyl-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

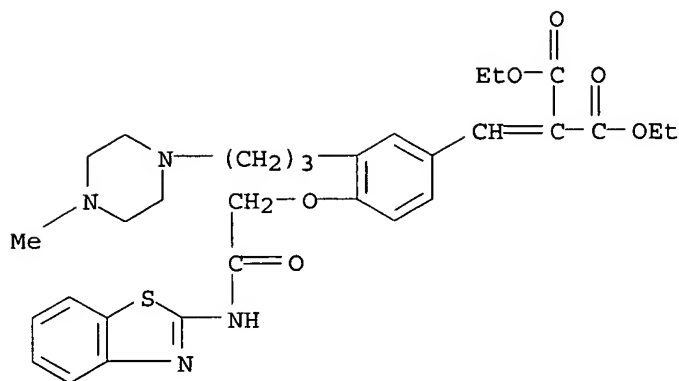
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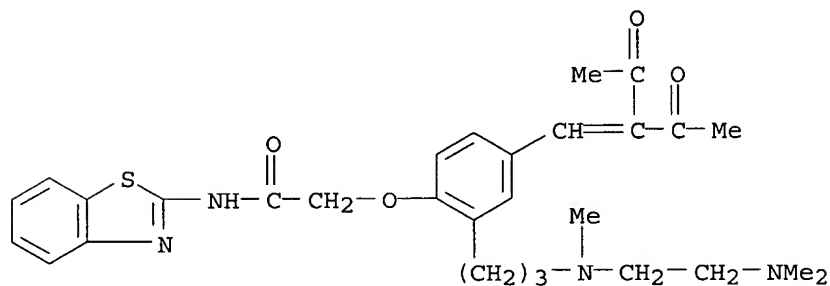
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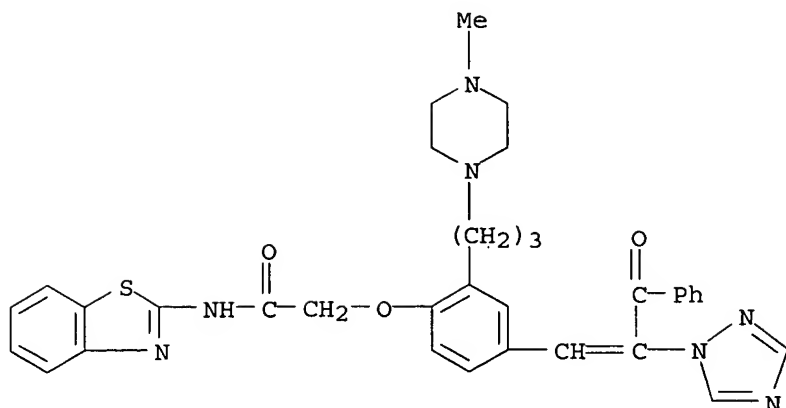
● 2 HCl

RN 215507-43-0 HCAPLUS  
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● 2 HCl

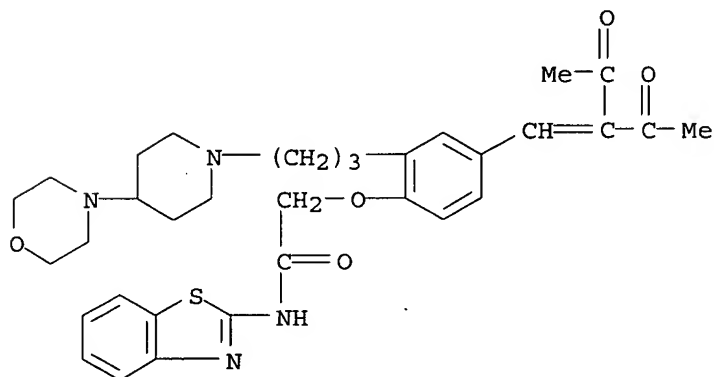
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●3 HCl

RN 215507-60-1 HCAPLUS

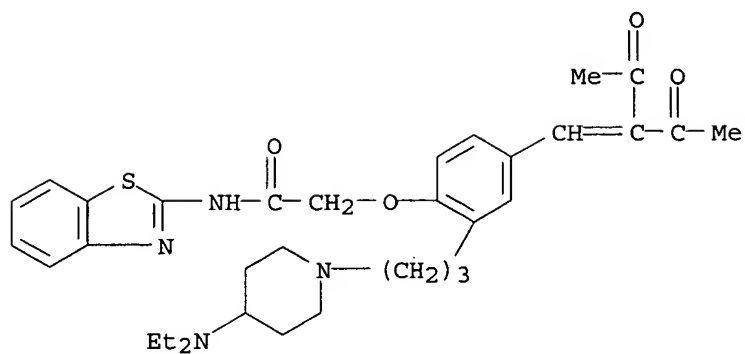
CN Acetamide, 2-[4-(2-acetyl-3-oxo-1-butenyl)-2-[3-[4-(4-morpholinyl)-1-piperidinyl]propyl]phenoxy]-N-2-benzothiazolyl-, trihydrochloride (9CI) (CA INDEX NAME)



●3 HCl

RN 215507-61-2 HCAPLUS

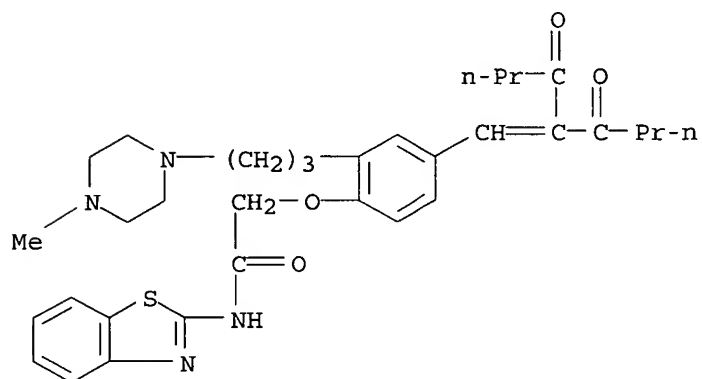
CN Acetamide, 2-[4-(2-acetyl-3-oxo-1-butenyl)-2-[3-[4-(diethylamino)-1-piperidinyl]propyl]phenoxy]-N-2-benzothiazolyl-, trihydrochloride (9CI) (CA INDEX NAME)



● 3 HCl

RN 215507-65-6 HCAPLUS

CN Acetamide, N-2-benzothiazolyl-2-[2-[3-(4-methyl-1-piperazinyl)propyl]-4-[3-oxo-2-(1-oxobutyl)-1-hexenyl]phenoxy]-, trihydrochloride (9CI) (CA INDEX NAME)

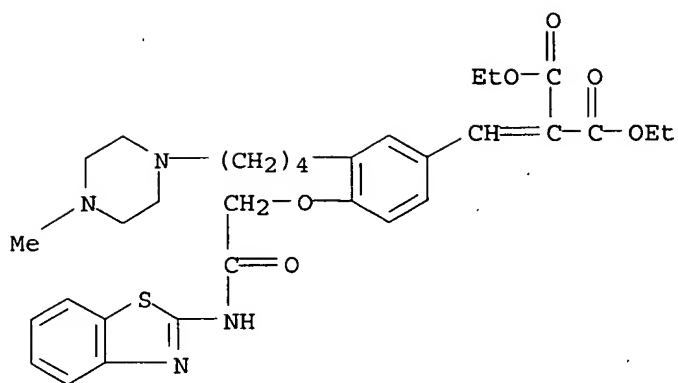


● 3 HCl

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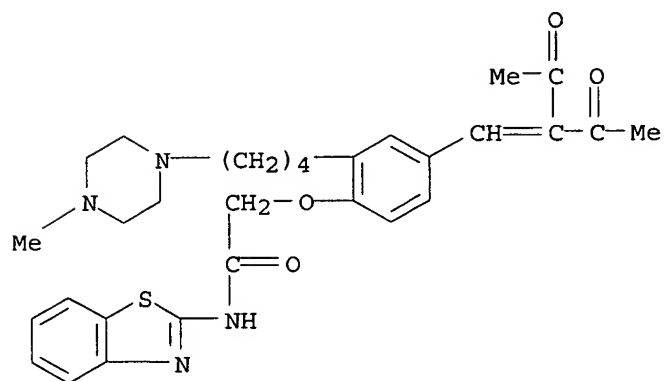
CN Propanedioic acid, [[4-[2-(2-benzothiazolylamino)-2-oxoethoxy]-3-[4-(4-methyl-1-piperazinyl)butyl]phenyl]methylene]-, diethyl ester, trihydrochloride (9CI) (CA INDEX NAME)





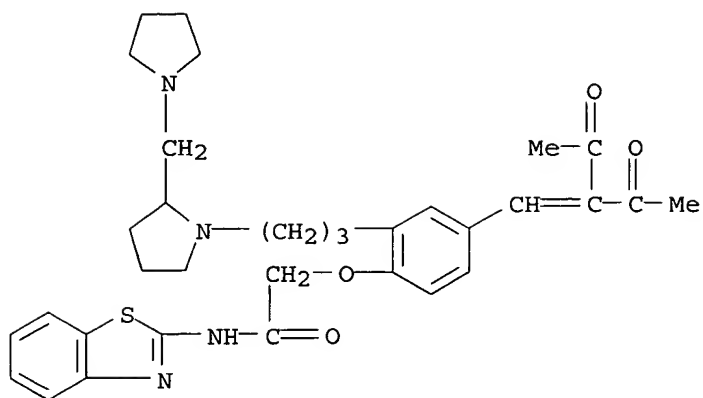
● 3 HCl

RN 215507-76-9 HCAPLUS  
 CN Acetamide, 2-[4-(2-acetyl-3-oxo-1-butenyl)-2-[4-(4-methyl-1-piperazinyl)butyl]phenoxy]-N-2-benzothiazolyl-, trihydrochloride (9CI) (CA INDEX NAME)



● 3 HCl

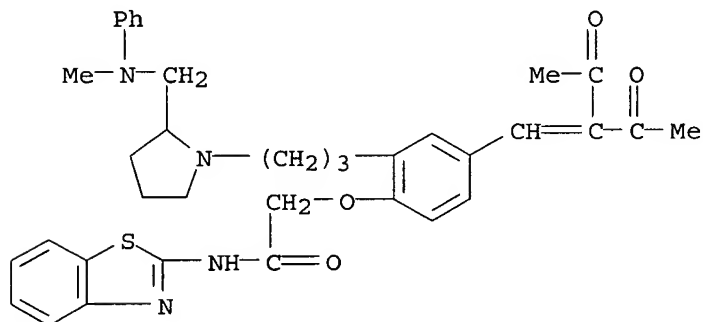
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● 3 HCl

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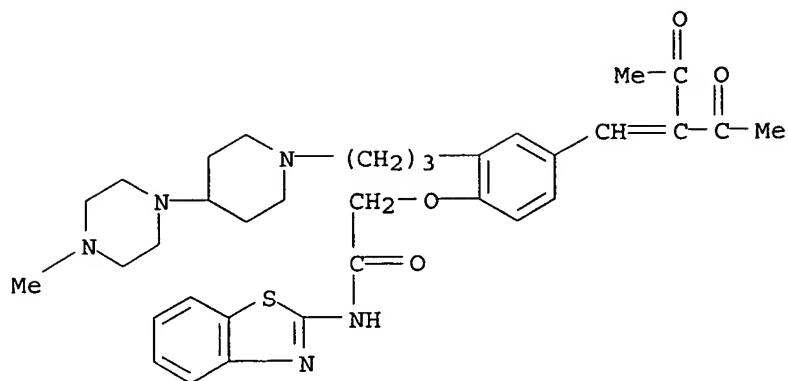
CN Acetamide, 2-[4-(2-acetyl-3-oxo-1-butenyl)-2-[3-[2-[(methylphenylamino)methyl]-1-pyrrolidinyl]propyl]phenoxy]-N-2-benzothiazolyl-, trihydrochloride (9CI) (CA INDEX NAME)



● 3 HCl

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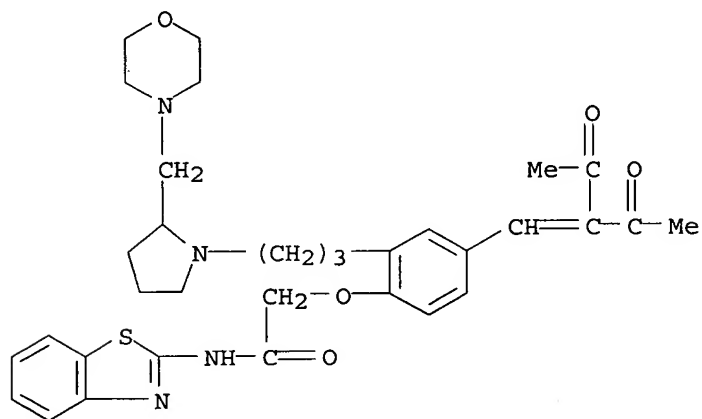
CN Acetamide, 2-[4-(2-acetyl-3-oxo-1-butenyl)-2-[3-[4-(4-methyl-1-piperazinyl)-1-piperidinyl]propyl]phenoxy]-N-2-benzothiazolyl-, tetrahydrochloride (9CI) (CA INDEX NAME)



● 4 HCl

RN 215507-81-6 HCAPLUS

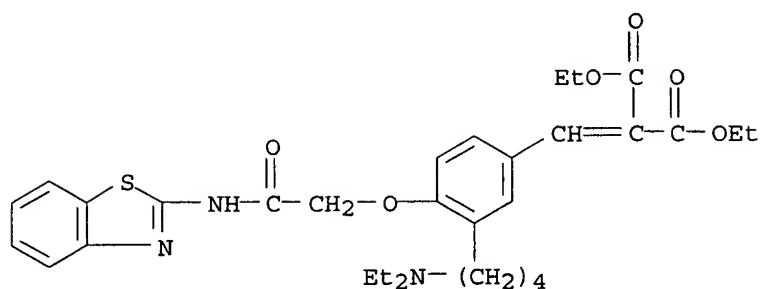
CN Acetamide, 2-[4-(2-acetyl-3-oxo-1-butenyl)-2-[3-[2-(4-morpholinylmethyl)-1-pyrrolidinyl]propyl]phenoxy]-N-2-benzothiazolyl-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

RN 215507-82-7 HCAPLUS

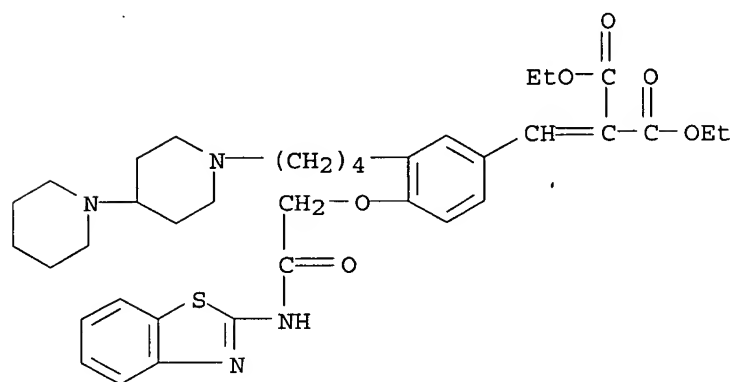
CN Propanedioic acid, [[4-[2-(2-benzothiazolylamino)-2-oxoethoxy]-3-[4-(diethylamino)butyl]phenyl]methylene]-, diethyl ester, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 215507-83-8 HCAPLUS

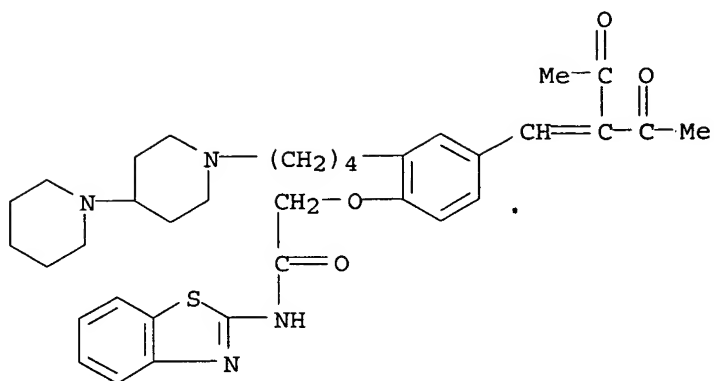
CN Propanedioic acid, [[4-[2-(2-benzothiazolylamino)-2-oxoethoxy]-3-(4-[1,4'-bipiperidin]-1'-ylbutyl)phenyl]methylene]-, diethyl ester, trihydrochloride (9CI) (CA INDEX NAME)



● 3 HCl

RN 215507-85-0 HCAPLUS

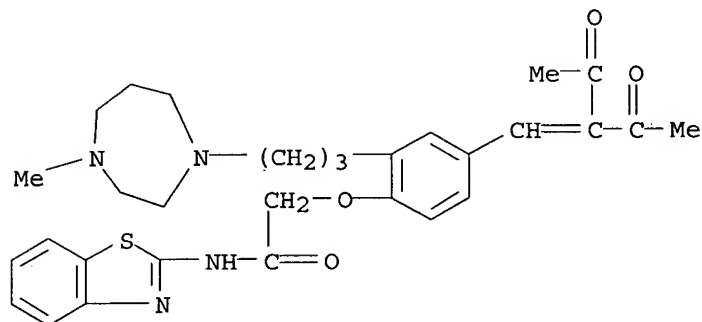
CN Acetamide, 2-[4-(2-acetyl-3-oxo-1-butenyl)-2-(4-[1,4'-bipiperidin]-1'-ylbutyl)phenoxy]-N-2-benzothiazolyl-, trihydrochloride (9CI) (CA INDEX NAME)



●3 HCl

RN 215507-86-1 HCAPLUS

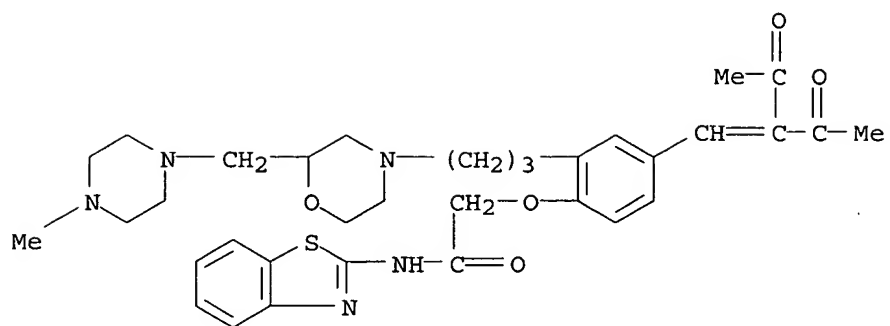
CN Acetamide, 2-[4-(2-acetyl-3-oxo-1-butenyl)-2-[3-(hexahydro-4-methyl-1H-1,4-diazepin-1-yl)propyl]phenoxy]-N-2-benzothiazolyl-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 215507-87-2 HCAPLUS

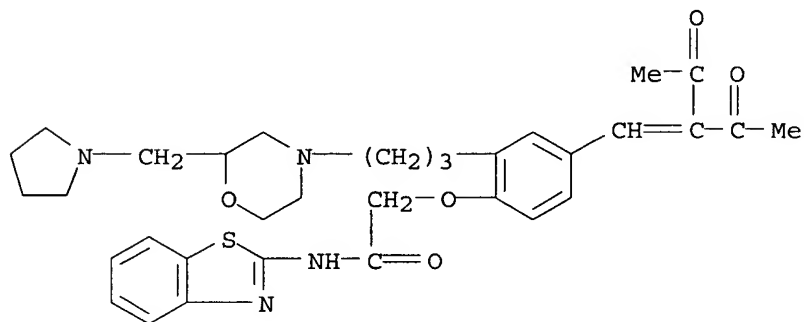
CN Acetamide, 2-[4-(2-acetyl-3-oxo-1-butenyl)-2-[3-[2-[(4-methyl-1-piperazinyl)methyl]-4-morpholinyl]propyl]phenoxy]-N-2-benzothiazolyl-, tetrahydrochloride (9CI) (CA INDEX NAME)



● 4 HCl

RN 215507-88-3 HCAPLUS

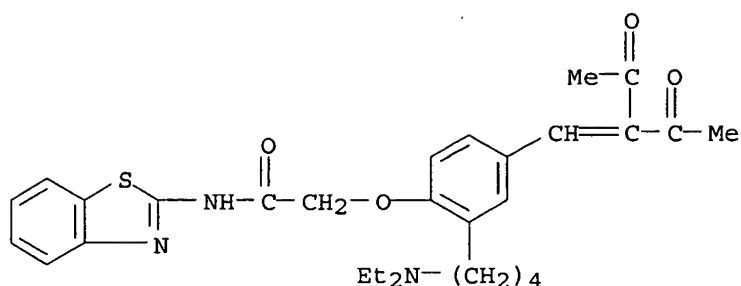
CN Acetamide, 2-[4-(2-acetyl-3-oxo-1-butenyl)-2-[3-[2-(1-pyrrolidinylmethyl)-4-morpholinyl]propyl]phenoxy]-N-2-benzothiazolyl-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

RN 215507-89-4 HCAPLUS

CN Acetamide, 2-[4-(2-acetyl-3-oxo-1-butenyl)-2-[4-(diethylamino)butyl]phenoxy]-N-2-benzothiazolyl-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

- IC ICM C07C233-18  
ICS C07C235-80; C07C259-06; C07C325-00; C07D277-44; C07D277-82;  
C07D403-12; C07D417-12; C07D417-14; C07D521-00; A61K031-425
- CC 25-1 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)  
Section cross-reference(s): 1, 27, 28, 63
- IT Allergy inhibitors  
Anti-Alzheimer's agents  
Anti-ischemic agents  
Antiarthritics  
**Antidiabetic agents**  
Antirheumatic agents  
Antitumor agents  
Autoimmune disease  
(preparation of benzenes as protein kinase C inhibitors for  
treatment of diseases)
- IT 215506-65-3P 215507-40-7P  
(preparation of benzenes as protein kinase C inhibitors for  
treatment of diseases)
- IT 1620-53-7P, 2-(Benzoylmethyl)pyridine 37910-79-5P 46720-41-6P  
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(preparation of benzenes as protein kinase C inhibitors for  
treatment of diseases)

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 (preparation of benzenes as protein kinase C inhibitors for  
 treatment of diseases)

L32 ANSWER 32 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:169451 HCAPLUS

DOCUMENT NUMBER: 128:230241

TITLE: Preparation of carbazole derivs. as selective  
 $\beta$ 3 adrenergic agonists

INVENTOR(S): Crowell, Thomas A.; Evrard, Deborah A.; Jones,  
 Charles D.; Muehl, Brian S.; Rito, Christopher  
 J.; Shuker, Anthony J.; Thorpe, Andrew J.;  
 Thrasher, Kenneth J.

PATENT ASSIGNEE(S): Eli Lilly and Company, USA; Crowell, Thomas  
 A.; Evrard, Deborah A.; Jones, Charles D.;  
 Muehl, Brian S.; Rito, Christopher J.; Shuker,  
 Anthony J.; Thorpe, Andrew J.; Thrasher,  
 Kenneth J.

SOURCE: PCT Int. Appl., 135 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9809625	A1	19980312	WO 1997-US15230	1997 0828

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 LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU,  
 SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN,  
 YU, ZW  
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GA, GN, ML, MR, NE, SN, TD, TG

EP 827746 A1 19980311 EP 1997-306613

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EP 827746 B1 20020403

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PRIORITY APPLN. INFO.:

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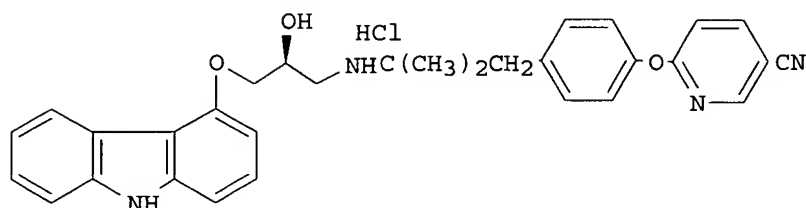
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US 2002-120302 A1  
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OTHER SOURCE(S): MARPAT 128:230241  
GI



AB Title compds. R1X1CH(OH)CH2N(R3)C(R5R6)X2X3R4 I (X1 = OCH2, SCH2, bond; X2 = bond, alkylene; X3 = O, S, bond; R1 = fused heterocycle; R3 = H, alkyl; R4 = (un)substituted heterocycle, naphthyl, etc.; R5 = H, alkyl; R6 = H, alkyl CO-O-alkyl; R5-R6 = cycloalkyl; R6-X2 = cycloalkyl; etc.) are prepared for selective  $\beta_3$  receptor agonists which are useful in the treatment of Type II **diabetes** and obesity, comprising administering to mammal. The title compound II was prepared from (2S)-(+)-4-(oxiranylmethoxy)-9H-carbazole and 2-(4-(2-amino-2-methylpropyl)phenoxy)-5-pyridinecarbonitrile which was prepared from 2-fluoropyridine and 4-(2-amino-2-methylpropyl)phenol.

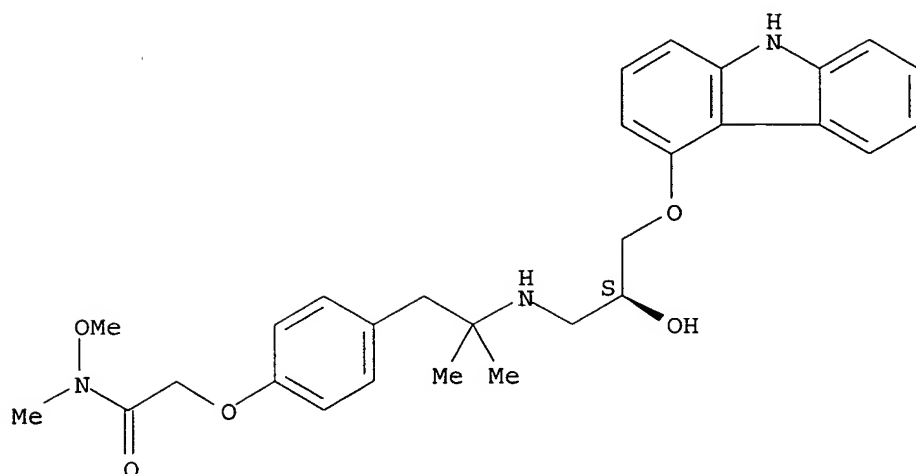
IT **204593-17-9P**

(preparation of carbazole derivs. as adrenergic agonists)

RN 204593-17-9 HCAPLUS

CN Acetamide, 2-[4-[2-[3-(9H-carbazol-4-yloxy)-2-hydroxypropyl]amino]-2-methylpropyl]phenoxy]-N-methoxy-N-methyl-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IC ICM A61K031-40

ICS A61K031-44; C07D209-82; C07D209-88; C07D401-12

CC 27-11 (Heterocyclic Compounds (One Hetero Atom))

Section cross-reference(s): 1, 63

IT **Antidiabetic agents**

(preparation of carbazole derivs. as)

IT	95094-00-1P	204592-55-2P	204592-56-3P	204592-57-4P
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	204592-83-6P	204592-84-7P	204592-85-8P	204592-86-9P
	204592-87-0P	204592-88-1P	204592-89-2P	204592-90-5P
	204592-91-6P	204592-92-7P	204592-93-8P	204592-94-9P
	204592-95-0P	204592-96-1P	204592-97-2P	204592-98-3P
	204592-99-4P	204593-00-0P	204593-01-1P	204593-02-2P
	204593-03-3P	204593-04-4P	204593-05-5P	204593-06-6P
	204593-07-7P	204593-08-8P	204593-09-9P	204593-10-2P
	204593-11-3P	204593-12-4P	204593-13-5P	204593-14-6P
	204593-15-7P	204593-16-8P	<b>204593-17-9P</b>	204593-18-0P
	204593-19-1P	204593-20-4P	204593-21-5P	204593-22-6P
	204593-23-7P	204593-24-8P	204593-25-9P	204593-26-0P
	204593-27-1P	204593-28-2P	204593-29-3P	204593-30-6P
	204593-31-7P	204593-32-8P	204593-33-9P	204593-34-0P
	204593-35-1P	204593-36-2P	204593-37-3P	204593-38-4P
	204637-55-8P	204773-65-9P		

(preparation of carbazole derivs. as adrenergic agonists)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE  
FOR THIS RECORD. ALL CITATIONS AVAILABLE  
IN THE RE FORMAT

L32 ANSWER 33 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1986:5623 HCAPLUS

DOCUMENT NUMBER: 104:5623

TITLE: Tertiary phenethylamines

INVENTOR(S): Berge, John; Hindley, Richard Mark

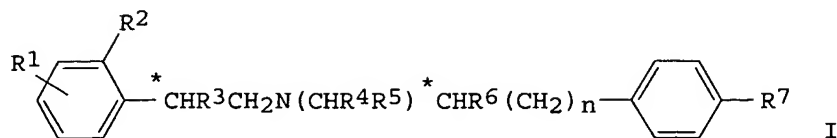
PATENT ASSIGNEE(S): Beecham Group PLC, UK

SOURCE: Eur. Pat. Appl., 44 pp.

DOCUMENT TYPE: CODEN: EPXXDW  
 LANGUAGE: Patent  
 FAMILY ACC. NUM. COUNT: English  
 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 142102	A2	19850522	EP 1984-113089	1984 1030
EP 142102	A3	19860430	<--	
EP 142102	B1	19870923		
R: BE, CH, DE, FR, GB, IT, LI, NL, SE				
AU 8434925	A1	19850509	AU 1984-34925	1984 1102
AU 580972	B2	19890209	<--	
JP 60112744	A2	19850619	JP 1984-232241	1984 1102
ZA 8408570	A	19850828	ZA 1984-8570	1984 1102
ES 537359	A1	19851216	ES 1984-537359	1984 1102
CA 1246083	A1	19881206	CA 1984-466978	1984 1102
ES 545776	A1	19860116	ES 1985-545776	1985 0731
ES 545777	A1	19860601	ES 1985-545777	1985 0731
US 4803293	A	19890207	US 1987-17002	1987 0218
PRIORITY APPLN. INFO.:			GB 1983-29490	A 1983 1104
			GB 1983-34294	A 1983 1222
			US 1984-667757	A1 1984 1102

OTHER SOURCE(S): MARPAT 104:5623  
GI



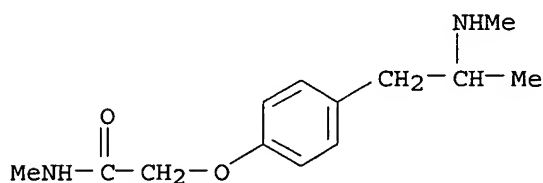
AB Phenethyl amines I [R1 = H, halo, CF3; R2 = H, halo; R3 = OH, alkoxy, amino; R4 = H, alkyl; R5 = H, (un)substituted alkyl, alkenyl, alkynyl; R6 = H, Me; R7 = (esters and amides of) CO2H, carboxyalkyloxy, (un)substituted alkoxy; the asterisks indicate potential optically active centers; n = 1, 2], useful as antihyperglycemic and antiobesity agents, were prepared. Thus, (RR,SS)-3-ClC6H4C6H4CH(OH)NR8CHMeC6H4(OCH2CO2Me)-4 (II; R8 = H) was N-alkylated with BrCH2CH2OH to give II (R8 = CH2CH2OH) (III). At 22.9 mg/kg orally, III increased the energy expenditure of mice by 167% during a 3 h period. At 0.5  $\mu$ mol/kg orally in mice, III reduced blood glucose by 52% during a 2 h period following administration of glucose s.c.

IT 99386-66-0P 99386-67-1P

(preparation and alkylation of, with bromoacetophenone)

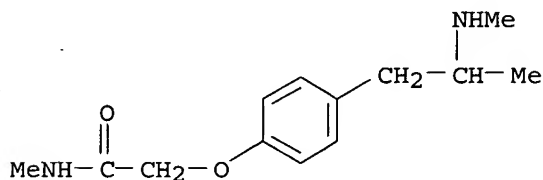
RN 99386-66-0 HCAPLUS

CN Acetamide, N-methyl-2-[4-[2-(methylamino)propyl]phenoxy]- (9CI)  
(CA INDEX NAME)



RN 99386-67-1 HCAPLUS

CN Acetamide, N-methyl-2-[4-[2-(methylamino)propyl]phenoxy]-, monohydrochloride (9CI) (CA INDEX NAME)



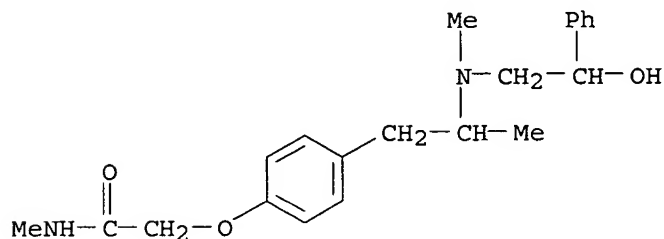
● HCl

IT 99386-50-2P 99404-59-8P

(preparation and hypoglycemic and antiobesity activity of)

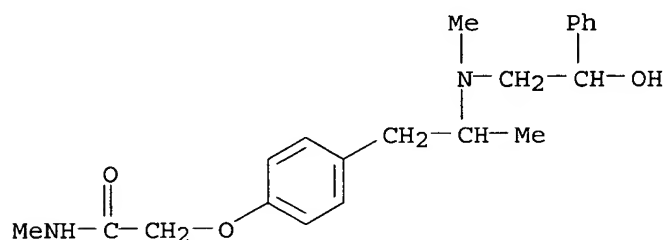
RN 99386-50-2 HCAPLUS

CN Acetamide, 2-[4-[2-[(2-hydroxy-2-phenylethyl)methylamino]propyl]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



RN 99404-59-8 HCAPLUS

CN Acetamide, 2-[4-[2-[(2-hydroxy-2-phenylethyl)methylamino]propyl]phenoxy]-N-methyl-, monohydrochloride (9CI) (CA INDEX NAME)



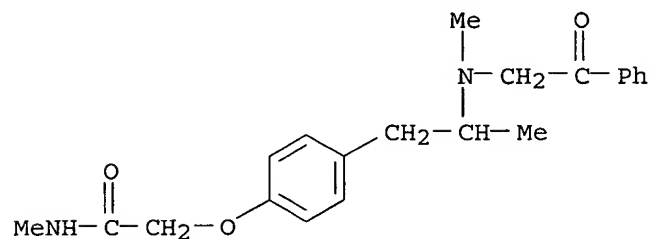
● HCl

IT 99386-65-9P

(preparation and reduction of)

RN 99386-65-9 HCAPLUS

CN Acetamide, N-methyl-2-[4-[2-[methyl(2-oxo-2-phenylethyl)amino]propyl]phenoxy]- (9CI) (CA INDEX NAME)



IC ICM C07C101-12

ICS C07C101-18; C07C101-30; C07C103-78; C07C099-00; C07D295-12

CC 25-4 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)  
Section cross-reference(s): 1

IT Antidiabetics and Hypoglycemics

Appetite depressants and Antiobesity agents  
(tertiary phenthylamine derivs.)

IT 99386-66-0P 99386-67-1P  
(preparation and alkylation of, with bromoacetophenone)

IT 99386-28-4P 99386-32-0P 99386-33-1P 99386-34-2P  
99386-35-3P 99386-36-4P 99386-37-5P 99386-38-6P  
99386-39-7P 99386-40-0P 99386-41-1P 99386-42-2P  
99386-43-3P 99386-44-4P 99386-48-8P 99386-49-9P  
99386-50-2P 99386-51-3P 99386-52-4P 99386-53-5P  
99386-54-6P 99386-55-7P 99386-56-8P 99386-57-9P  
99386-58-0P 99386-59-1P 99386-60-4P 99386-61-5P  
99386-63-7P 99386-64-8P 99386-68-2P 99386-69-3P  
99386-70-6P 99386-71-7P 99386-72-8P 99386-73-9P  
99397-34-9P 99404-59-8P 99404-60-1P  
(preparation and hypoglycemic and antiobesity activity of)

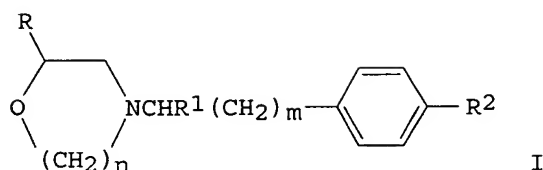
IT 99386-65-9P  
(preparation and reduction of)

L32 ANSWER 34 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 1985:523489 HCAPLUS  
DOCUMENT NUMBER: 103:123489  
TITLE: Morpholine derivatives  
INVENTOR(S): Cantello, Barrie Christian Charles  
PATENT ASSIGNEE(S): Beecham Group PLC, UK  
SOURCE: Eur. Pat. Appl., 36 pp.  
CODEN: EPXXDW  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 140359	A1	19850508	EP 1984-113014	1984 1029
EP 140359	B1	19890125		
R: CH, DE, FR, GB, IT, LI, NL				
US 4607033	A	19860819	US 1984-666818	1984 1031
JP 60112778	A2	19850619	JP 1984-231130	1984 1101
JP 06004604	B4	19940119		
US 4665072	A	19870512	US 1986-865348	1986 0521
US 4783460	A	19881108	US 1987-26893	1987 0317
PRIORITY APPLN. INFO.:			GB 1983-29247	A 1983 1102

<--  
 GB 1984-4047 A 1984  
 0216  
 <--  
 US 1984-666818 A3 1984  
 1031  
 <--  
 US 1986-865348 A3 1986  
 0521  
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OTHER SOURCE(S): MARPAT 103:123489  
 GI



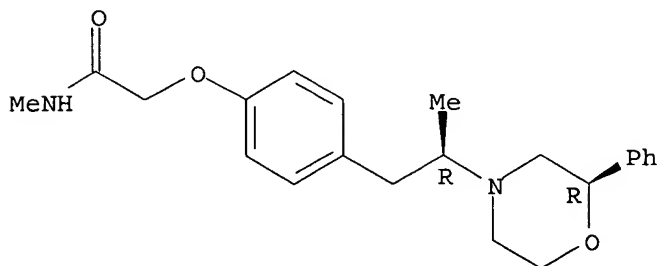
AB Morpholines and perhydrooxazepines I [ $n = 2, 3$ ;  $R = \text{Ph}$ , halophenyl, (trifluoromethyl)phenyl, 2-benzofuryl;  $R_1 = \text{H}$ , Me;  $m = 1, 2$ ;  $R_2 = \text{CO}_2\text{H}$ , esterified  $\text{CO}_2\text{H}$ , carbamoyl, carboxyalkoxy, esterified carboxyalkoxy, carbamoylalkoxy, aminoalkoxy, hydroxyalkoxy, alkoxyalkoxy], which were prepared, exhibited **antidiabetic** activity. 2-Phenylmorpholine was stirred with 4-( $\text{MeCOCH}_2$ ) $\text{C}_6\text{H}_4\text{OCH}_2\text{CO}_2\text{Me}$  and  $\text{NaB}(\text{CN})\text{H}_3$  in MeOH, and the mixture was worked up to give I ( $n = 2$ ,  $R = \text{Ph}$ ,  $R_1 = \text{Me}$ ,  $m = 1$ ,  $R_2 = \text{OCH}_2\text{CO}_2\text{Me}$ ).

IT 98235-44-0P 98235-45-1P 98235-56-4P  
 98235-60-0P 98235-61-1P  
 (preparation and **antidiabetic** activity of)

RN 98235-44-0 HCAPLUS

CN Acetamide, N-methyl-2-[4-[2-(2-phenyl-4-morpholinyl)propyl]phenoxy]-, monohydrochloride, ( $R^*, R^*$ )-(9CI)  
 (CA INDEX NAME)

Relative stereochemistry.

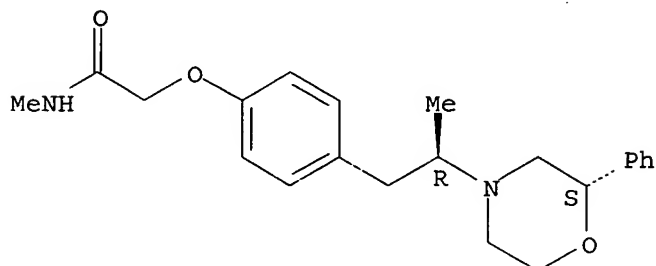


● HCl



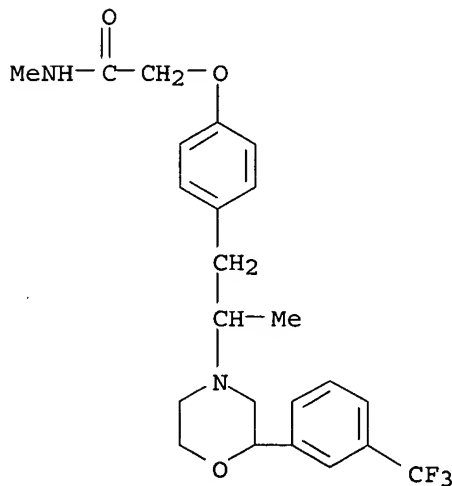
RN 98235-45-1 HCAPLUS  
 CN Acetamide, N-methyl-2-[4-[2-(2-phenyl-4-morpholinyl)propyl]phenoxy]-, monohydrochloride, (R\*,S\*)- (9CI)  
 (CA INDEX NAME)

Relative stereochemistry.



● HCl

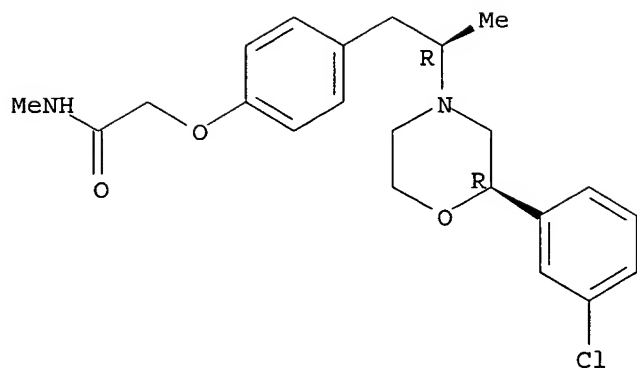
RN 98235-56-4 HCAPLUS  
 CN Acetamide, N-methyl-2-[4-[2-[2-[3-(trifluoromethyl)phenyl]-4-morpholinyl]propyl]phenoxy]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 98235-60-0 HCAPLUS  
 CN Acetamide, 2-[4-[2-[2-(3-chlorophenyl)-4-morpholinyl]propyl]phenoxy]-N-methyl-, dihydrochloride, (R\*,R\*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.

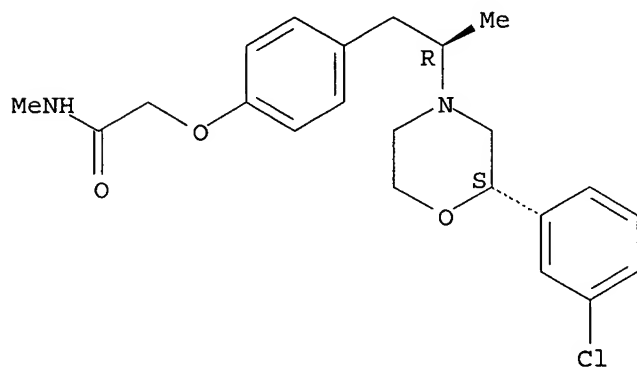


● 2 HCl

RN 98235-61-1 HCAPLUS

CN Acetamide, 2-[4-[2-[2-(3-chlorophenyl)-4-morpholinyl]propyl]phenoxy]-N-methyl-, dihydrochloride, (R\*,S\*)-(9CI) (CA INDEX NAME)

Relative stereochemistry.



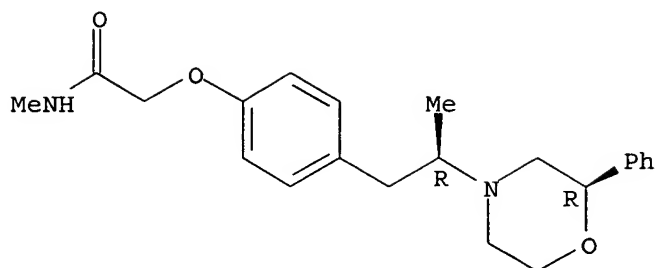
● 2 HCl

IT 98235-46-2P 98235-47-3P  
(preparation of)

RN 98235-46-2 HCAPLUS

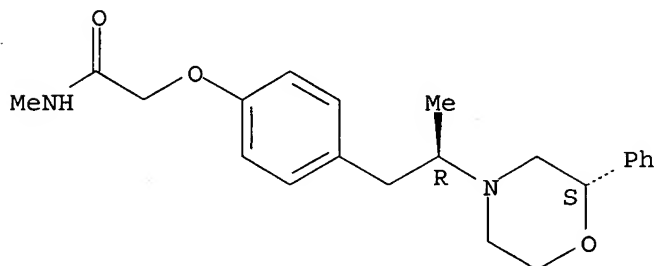
CN Acetamide, N-methyl-2-[4-[2-(2-phenyl-4-morpholinyl)propyl]phenoxy]-, (R\*,R\*)-(9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 98235-47-3 HCAPLUS  
 CN Acetamide, N-methyl-2-[4-[2-(2-phenyl-4-morpholinyl)propyl]phenoxy]-, (R\*,S\*)- (9CI) (CA INDEX NAME)

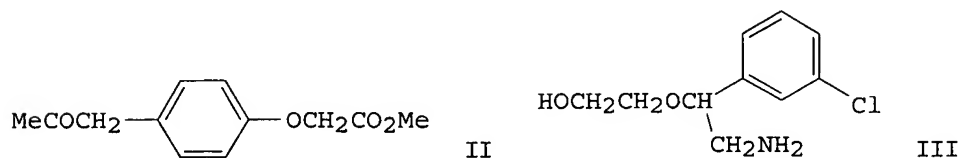
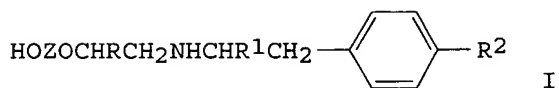
Relative stereochemistry.



IC ICM C07D265-30  
 ICS C07D267-10; C07D413-04; A61K031-535; A61K031-55  
 CC 28-13 (Heterocyclic Compounds (More Than One Hetero Atom))  
 ST morpholine phenylisopropyl prepn **antidiabetic**;  
 phenylisopropylmorpholine prepn **antidiabetic**  
 IT **Antidiabetics** and Hypoglycemics  
 IT 98235-40-6P 98235-41-7P **98235-44-0P**  
**98235-45-1P** 98235-48-4P 98235-49-5P 98235-52-0P  
**98235-56-4P** 98235-58-6P 98235-59-7P  
**98235-60-0P** **98235-61-1P** 98235-62-2P  
 98235-63-3P 98235-66-6P 98235-67-7P 98235-72-4P  
 (preparation and **antidiabetic** activity of)  
 IT 98235-42-8P 98235-43-9P **98235-46-2P**  
**98235-47-3P** 98235-50-8P 98235-51-9P 98235-54-2P  
 98235-64-4P 98235-65-5P 98235-69-9P 98235-70-2P  
 98235-73-5P  
 (preparation of)

L32 ANSWER 35 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1985:504687 HCAPLUS  
 DOCUMENT NUMBER: 103:104687  
 TITLE: 2-Phenylethylamine derivatives  
 PATENT ASSIGNEE(S): Beecham Group PLC, UK  
 SOURCE: Jpn. Kokai Tokkyo Koho, 15 pp.  
 CODEN: JKXXAF  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO. -----	KIND ---	DATE -----	APPLICATION NO. -----	DATE
JP 60067450	A2	19850417	JP 1984-170108	1984 0816
EP 139921	A1	19850508	<-- EP 1984-109391	1984 0808
EP 139921 R: BE, CH, DE, FR, GB, IT, LI, NL, SE	B1	19870325	<--	
AU 8431944	A1	19850221	AU 1984-31944	1984 0815
ZA 8406331	A	19850731	<-- ZA 1984-6331	1984 0815
US 4692465	A	19870908	<-- US 1984-640850	1984 0815
ES 535226	A1	19851101	<-- ES 1984-535226	1984 0816
PRIORITY APPLN. INFO.:			<-- GB 1983-22137	A 1983 0817
			<-- GB 1983-34293	A 1983 1222
OTHER SOURCE(S): GI		MARPAT 103:104687	<--	



AB Phenylethylamine derivs. (I; R = aryl, 2-benzofuryl; R<sup>1</sup> = H, Me; R<sup>2</sup> = HOCH<sub>2</sub>CH<sub>2</sub>O, MeNHCH<sub>2</sub>CH<sub>2</sub>O, MeO<sub>2</sub>CCH<sub>2</sub>O, H<sub>2</sub>NCOCH<sub>2</sub>O; etc.; Z = alkylene), effective hypoglycemics at 2.5-25.0 μmol/kg in mice

s.c., were prepared Thus, a mixture of 4.4 g II, 4.3 g III, and 50 mg Pt oxide in MeOH was treated with H, passed through kieselguhr, distilled in vacuo, and treated with HCl-Et<sub>2</sub>O to give a mixture of 56:44 diastereomeric I.HCl (R = 3-ClC<sub>6</sub>H<sub>4</sub>, R<sub>1</sub> = Me, R<sub>2</sub> = MeO<sub>2</sub>CCH<sub>2</sub>O).

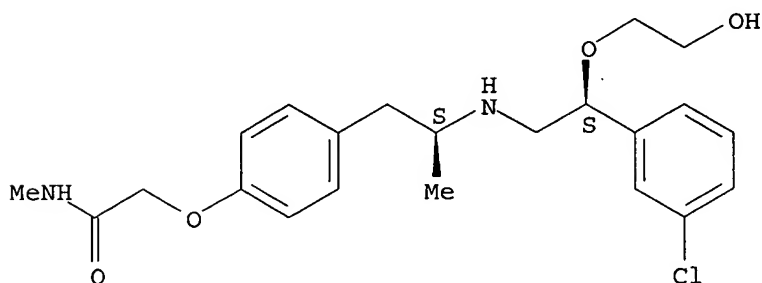
IT 97967-50-5P

(preparation and hypoglycemic activity of)

RN 97967-50-5 HCAPLUS

CN Acetamide, 2-[4-[2-[[2-(3-chlorophenyl)-2-(2-hydroxyethoxy)ethyl]amino]propyl]phenoxy]-N-methyl-, monohydrochloride, (R\*,R\*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



● HCl

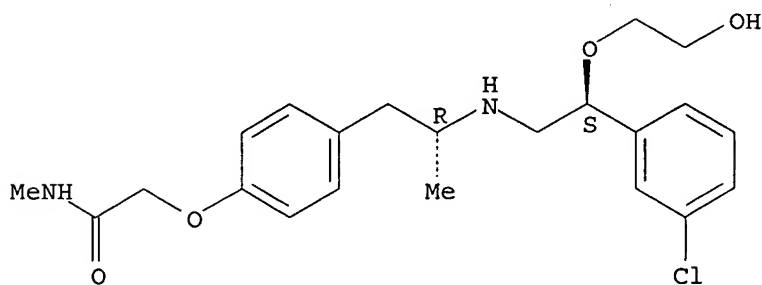
IT 97967-62-9P 97967-72-1P 97967-73-2P

(preparation of)

RN 97967-62-9 HCAPLUS

CN Acetamide, 2-[4-[2-[[2-(3-chlorophenyl)-2-(2-hydroxyethoxy)ethyl]amino]propyl]phenoxy]-N-methyl-, monohydrochloride, (R\*,S\*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.

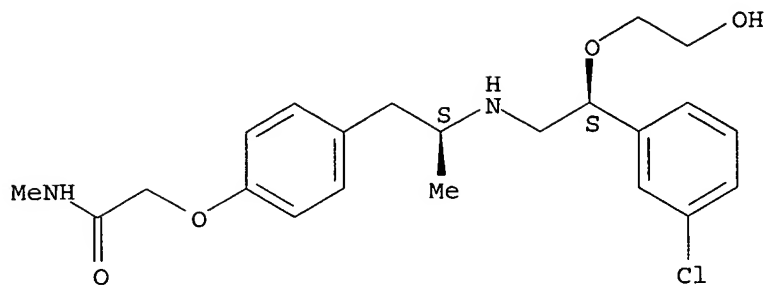


● HCl

RN 97967-72-1 HCAPLUS

CN Acetamide, 2-[4-[2-[[2-(3-chlorophenyl)-2-(2-hydroxyethoxy)ethyl]amino]propyl]phenoxy]-N-methyl-, (R\*,R\*)- (9CI) (CA INDEX NAME)

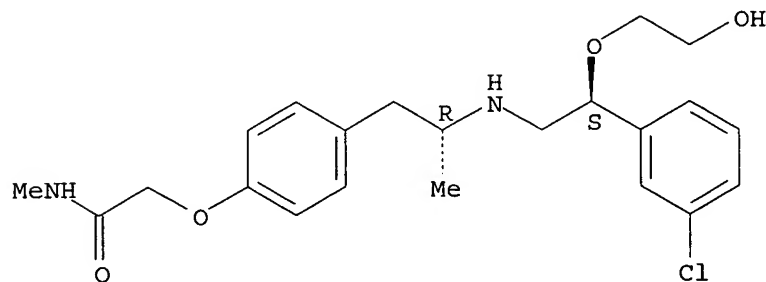
Relative stereochemistry.



RN 97967-73-2 HCAPLUS

CN Acetamide, 2-[4-[2-[[2-(3-chlorophenyl)-2-(2-hydroxyethoxy)ethyl]amino]propyl]phenoxy]-N-methyl-, (R\*,S\*)-(9CI) (CA INDEX NAME)

Relative stereochemistry.



IC ICM C07C093-04

ICS A61K031-135; A61K031-165; A61K031-195; A61K031-215;  
A61K031-34; C07C093-14; C07D295-08; C07D307-81

CC 25-4 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)  
Section cross-reference(s): 1

IT **Antidiabetics** and Hypoglycemics  
(phenylethylamine derivs.)

IT 97967-49-2P **97967-50-5P** 97967-51-6P 97967-52-7P  
97967-53-8P 97967-54-9P 97967-55-0P 97967-56-1P  
97967-57-2P

(preparation and hypoglycemic activity of)

IT 97967-30-1P 97967-31-2P 97967-32-3P 97967-58-3P  
97967-59-4P 97967-60-7P 97967-61-8P **97967-62-9P**  
97967-63-0P 97967-64-1P 97967-65-2P 97967-66-3P  
97967-67-4P 97967-68-5P 97967-69-6P 97967-70-9P  
97967-71-0P **97967-72-1P 97967-73-2P**  
97967-74-3P 97967-75-4P 97967-76-5P 97967-77-6P  
97967-78-7P 97967-79-8P 97967-80-1P 97967-81-2P  
97967-82-3P 97985-45-0P

(preparation of)

L32 ANSWER 36 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1985:148865 HCAPLUS

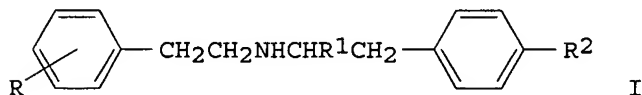
DOCUMENT NUMBER: 102:148865

TITLE: Pharmaceutically active 2-phenylethylamine  
derivatives

INVENTOR(S): Cantello, Barrie Christian Charles; Hindley,

PATENT ASSIGNEE(S): Richard Mark  
 SOURCE: Beecham Group PLC, UK  
 PCT Int. Appl., 26 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	----	-----	-----	
WO 8404091	A1	19841025	WO 1984-GB101	1984 0327
			<--	
W: GB, JP, US RW: CH, DE, FR, GB, NL EP 140922	A1	19850515	EP 1984-901385	1984 0327
			<--	
R: CH, DE, FR, GB, LI, NL PRIORITY APPLN. INFO.:			GB 1983-10556	A 1983 0419
			<--	
OTHER SOURCE(S):	MARPAT 102:148865			
GI				

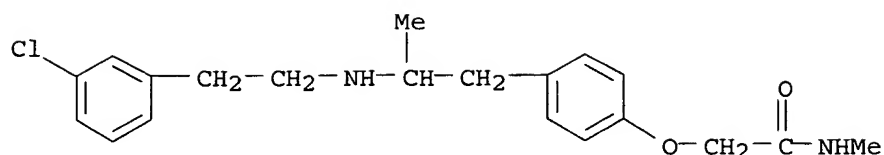


AB Amines I (R = H, halo, CF<sub>3</sub>; R<sub>1</sub> = H, Me; R<sub>2</sub> = ω-carboxyalkoxy, ω-hydroxy-, ω-alkoxy-, or ω-aminoalkoxy), which were prepared and showed **antidiabetic** activity. The reductive N-alkylation of 3-ClC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>CH<sub>2</sub>NH<sub>2</sub> by 4-(MeCOCH<sub>2</sub>)C<sub>6</sub>H<sub>4</sub>OCH<sub>2</sub>CO<sub>2</sub>Me gave I (R = 3-Cl, R<sub>1</sub> = Me, R<sub>2</sub> = OCH<sub>2</sub>CO<sub>2</sub>Me).

IT 95825-83-5P  
 (preparation and **antidiabetic** activity of)

RN 95825-83-5 HCAPLUS

CN Acetamide, 2-[4-[2-[[2-(3-chlorophenyl)ethyl]amino]propyl]phenoxy]-N-methyl-, monohydrochloride (9CI) (CA INDEX NAME)



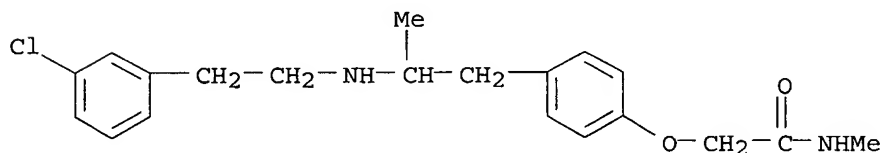
● HCl

IT 95825-84-6P

(preparation and reduction of)

RN 95825-84-6 HCAPLUS

CN Acetamide, 2-[[4-[[2-[(3-chlorophenyl)ethyl]amino]propyl]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)

IC C07C093-14; C07C103-34; A61K031-13; A61K031-19; A61K031-22;  
A61K031-16CC 25-4 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)  
Section cross-reference(s): 1ST phenethylamine phenylisopropyl prepn **antidiabetic**;  
**antidiabetic** phenylisopropylphenethylamine prepnIT **Antidiabetics** and Hypoglycemics  
(N-(phenylisopropyl)phenethylamines)IT 95825-81-3P 95825-83-5P 95825-85-7P  
(preparation and **antidiabetic** activity of)IT 95825-84-6P  
(preparation and reduction of)

L32 ANSWER 37 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1984:406799 HCAPLUS

DOCUMENT NUMBER: 101:6799

TITLE: 2-Aminoethyl ether derivatives, and their  
pharmaceutical compositions

INVENTOR(S): Cantello, Barrie Christian Charles

PATENT ASSIGNEE(S): Beecham Group PLC, UK

SOURCE: Eur. Pat. Appl., 87 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 99707	A1	19840201	EP 1983-303983	1983



0708

EP 99707 B1 19861210  
 R: BE, CH, DE, FR, GB, IT, LI, NL, SE  
 AU 8316826 A1 19840223 AU 1983-16826

1983  
0714

AU 557743 B2 19870108  
 ZA 8305126 A 19840627 ZA 1983-5126

1983  
0714

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0714

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0714

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1983  
0715

ES 524174 A1 19841116 ES 1983-524174

1983  
0715

PRIORITY APPLN. INFO.:

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1982  
0716

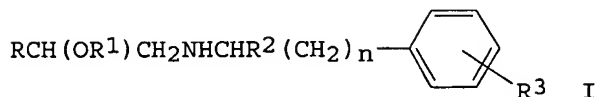
GB 1982-28753 A

1982  
1007

GB 1982-35672 A

1982  
1215

OTHER SOURCE(S): MARPAT 101:6799  
 GI



AB Amines I [R = Ph, alkyl-, halo-, or (trifluoromethyl)phenyl, PhOCH<sub>2</sub>, 2-benzofuryl; R<sup>1</sup> = alkyl, phenylalkyl; R<sup>2</sup> = H, Me; n = 1, 2; R<sup>3</sup> = CO<sub>2</sub>H, carboxyalkyl, carboxyalkenyl, hydroxyalkyl, hydroxyalkenyl, aminoalkyl, aminoalkenyl, alkoxy, alkylthio, alkylamino, hydroxyalkoxy, hydroxyalkylthio, hydroxyalkylamino, aminoalkoxy, aminoalkylthio, aminoalkylamino, Z<sub>1</sub>CO<sub>2</sub>H (Z = O, S, NH; Z<sub>1</sub> = alkylene, alkenylene)] were prepared, and they exhibited antidiabetic activity. A mixture of 4-

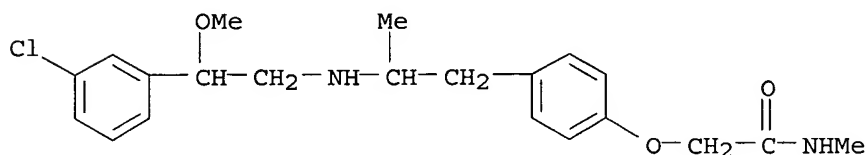
(MeCOCH<sub>2</sub>)C<sub>6</sub>H<sub>4</sub>OCH<sub>2</sub>CO<sub>2</sub>Me and 3-ClC<sub>6</sub>H<sub>4</sub>CH(OMe)CH<sub>2</sub>NH<sub>2</sub> in PhMe was refluxed 2 h, and the mixture was treated with Pt and H<sub>2</sub> to give I (R = 3-ClC<sub>6</sub>H<sub>4</sub>, R<sub>1</sub> = R<sub>2</sub> = Me, n = 1, R<sub>3</sub> = 4-OCH<sub>2</sub>CO<sub>2</sub>Me). Some I also showed antiinflammatory activity and inhibited blood platelet aggregation.

IT 90469-03-7P 90469-11-7P 90469-12-8P  
 90469-17-3P 90469-18-4P 90469-30-0P  
 90469-31-1P 90469-32-2P 90469-33-3P  
 90469-42-4P 90469-43-5P 90469-50-4P  
 90469-51-5P 90469-66-2P 90469-67-3P  
 90469-70-8P 90469-71-9P 90469-93-5P  
 90469-94-6P 90470-10-3P 90470-11-4P  
 90470-31-8P 90470-34-1P 90470-35-2P  
 90470-40-9P 90470-41-0P 90470-42-1P  
 90470-44-3P 90470-45-4P

(preparation and antidiabetic activity of)

RN 90469-03-7 HCAPLUS

CN Acetamide, 2-[4-[2-[2-(3-chlorophenyl)-2-methoxyethyl]amino]propyl]phenoxy]-N-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

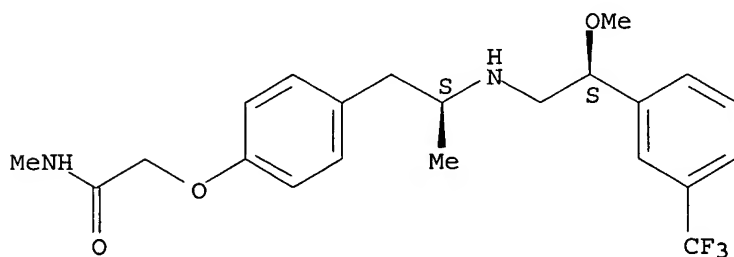


● HCl

RN 90469-11-7 HCAPLUS

CN Acetamide, 2-[4-[2-[2-[2-methoxy-2-[3-(trifluoromethyl)phenyl]ethyl]amino]propyl]phenoxy]-N-methyl-, monohydrochloride, (R\*,R\*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.

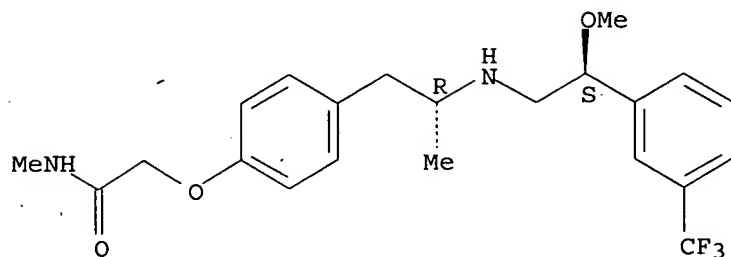


● HCl

RN 90469-12-8 HCAPLUS

CN Acetamide, 2-[4-[2-[2-[2-methoxy-2-[3-(trifluoromethyl)phenyl]ethyl]amino]propyl]phenoxy]-N-methyl-, monohydrochloride, (R\*,S\*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.

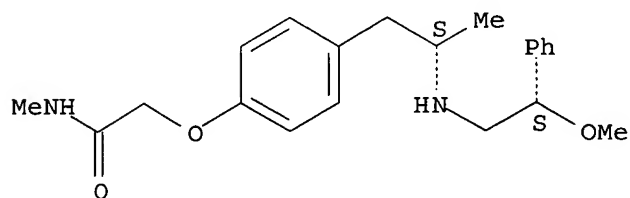


● HCl

RN 90469-17-3 HCAPLUS

CN Acetamide, 2-[4-[2-[(2-methoxy-2-phenylethyl)amino]propyl]phenoxy]-N-methyl-, monohydrochloride, (R\*,R\*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.

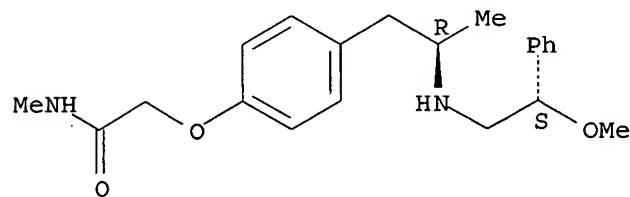


● HCl

RN 90469-18-4 HCAPLUS

CN Acetamide, 2-[4-[2-[(2-methoxy-2-phenylethyl)amino]propyl]phenoxy]-N-methyl-, monohydrochloride, (R\*,S\*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.

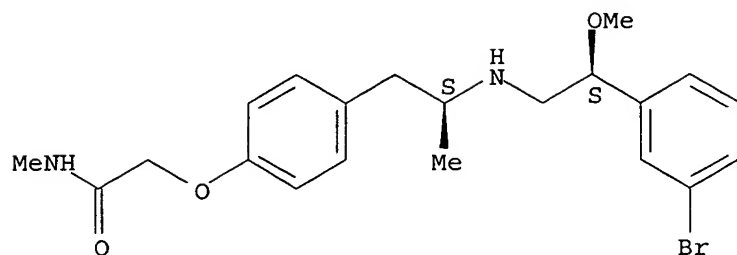


● HCl

RN 90469-30-0 HCAPLUS

CN Acetamide, 2-[4-[2-[[2-(3-bromophenyl)-2-methoxyethyl]amino]propyl]phenoxy]-N-methyl-, monohydrochloride, (R\*,R\*)- (9CI) (CA INDEX NAME)

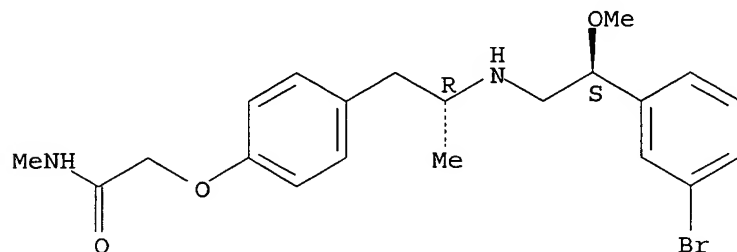
Relative stereochemistry.



● HCl

RN 90469-31-1 HCAPLUS  
 CN Acetamide, 2-[4-[2-[[2-(3-bromophenyl)-2-methoxyethyl]amino]propyl]phenoxy]-N-methyl-, monohydrochloride, (R\*,S\*)- (9CI) (CA INDEX NAME)

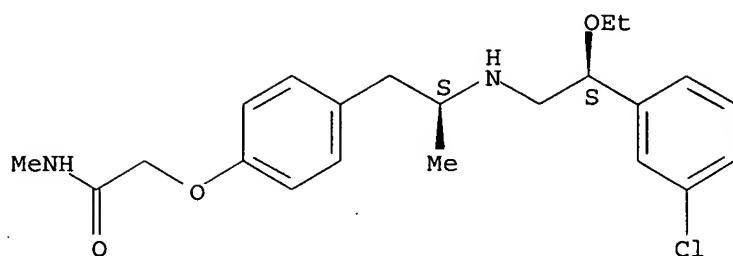
Relative stereochemistry.



● HCl

RN 90469-32-2 HCAPLUS  
 CN Acetamide, 2-[4-[2-[[2-(3-chlorophenyl)-2-ethoxyethyl]amino]propyl]phenoxy]-N-methyl-, monohydrochloride, (R\*,R\*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.

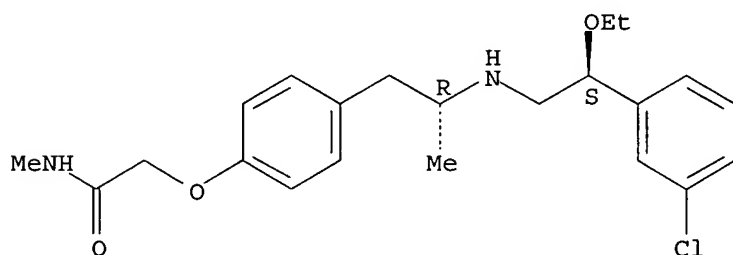


● HCl

RN 90469-33-3 HCAPLUS

CN Acetamide, 2-[4-[2-[[2-(3-chlorophenyl)-2-ethoxyethyl]amino]propyl]phenoxy]-N-methyl-, monohydrochloride, (R\*,S\*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.

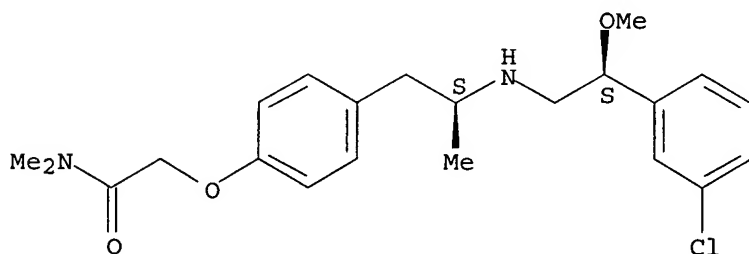


● HCl

RN 90469-42-4 HCAPLUS

CN Acetamide, 2-[4-[2-[[2-(3-chlorophenyl)-2-methoxyethyl]amino]propyl]phenoxy]-N,N-dimethyl-, monohydrochloride, (R\*,R\*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.

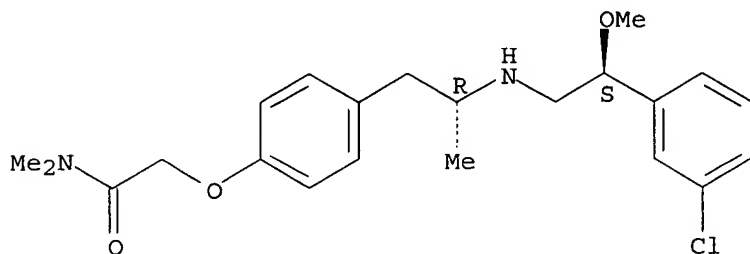


● HCl

RN 90469-43-5 HCAPLUS

CN Acetamide, 2-[4-[2-[[2-(3-chlorophenyl)-2-methoxyethyl]amino]propyl]phenoxy]-N,N-dimethyl-, monohydrochloride, (R\*,S\*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.

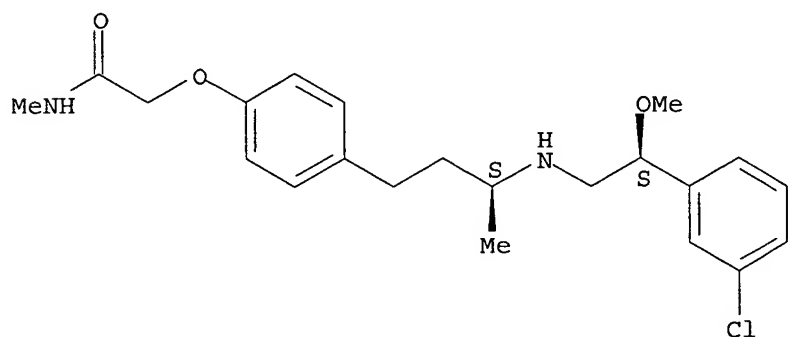


● HCl

RN 90469-50-4 HCAPLUS

CN Acetamide, 2-[4-[3-[[2-(3-chlorophenyl)-2-methoxyethyl]amino]butyl]phenoxy]-N-methyl-, monohydrochloride, (R\*,R\*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.

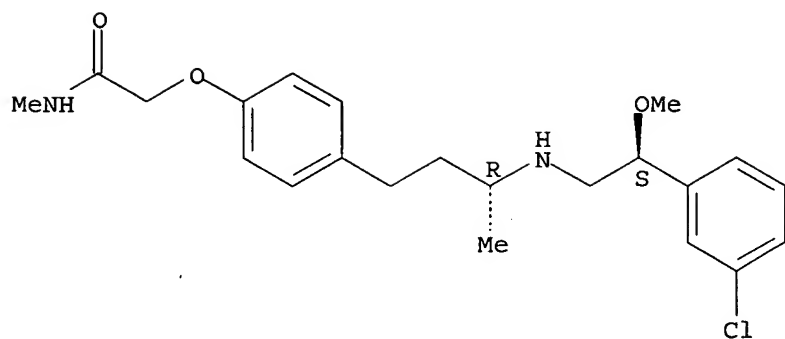


● HCl

RN 90469-51-5 HCAPLUS

CN Acetamide, 2-[4-[3-[[2-(3-chlorophenyl)-2-methoxyethyl]amino]butyl]phenoxy]-N-methyl-, monohydrochloride, (R\*,S\*)- (9CI) (CA INDEX NAME)

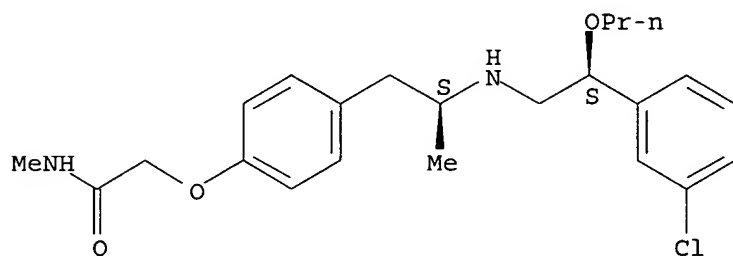
Relative stereochemistry.



● HCl

RN 90469-66-2 HCAPLUS  
 CN Acetamide, 2-[4-[2-[[2-(3-chlorophenyl)-2-propoxyethyl]amino]propyl]phenoxy]-N-methyl-, dihydrochloride, (R\*,R\*)- (9CI) (CA INDEX NAME)

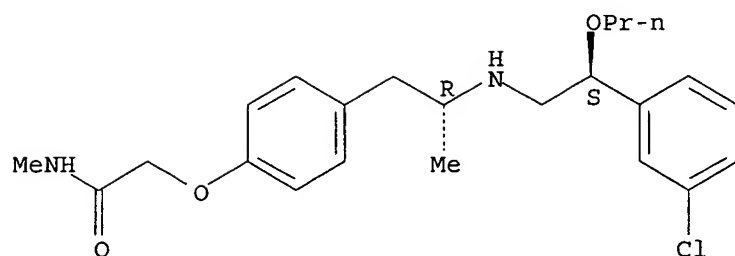
Relative stereochemistry.



● 2 HCl

RN 90469-67-3 HCAPLUS  
 CN Acetamide, 2-[4-[2-[[2-(3-chlorophenyl)-2-propoxyethyl]amino]propyl]phenoxy]-N-methyl-, dihydrochloride, (R\*,S\*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.

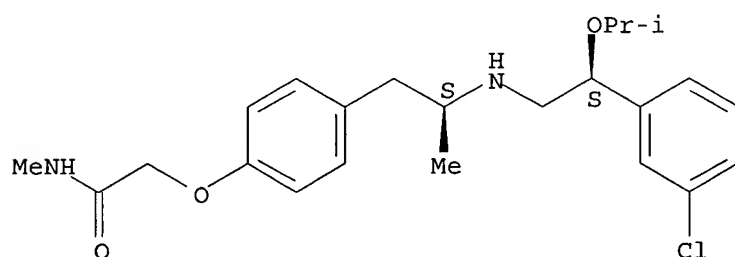


●2 HCl

RN 90469-70-8 HCAPLUS

CN Acetamide, 2-[4-[2-[[2-(3-chlorophenyl)-2-(1-methylethoxy)ethyl]amino]propyl]phenoxy]-N-methyl-, dihydrochloride, (R\*,R\*)-(9CI) (CA INDEX NAME)

Relative stereochemistry.

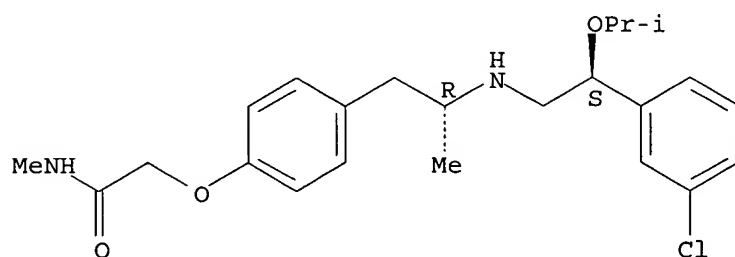


●2 HCl

RN 90469-71-9 HCAPLUS

CN Acetamide, 2-[4-[2-[[2-(3-chlorophenyl)-2-(1-methylethoxy)ethyl]amino]propyl]phenoxy]-N-methyl-, dihydrochloride, (R\*,S\*)-(9CI) (CA INDEX NAME)

Relative stereochemistry.



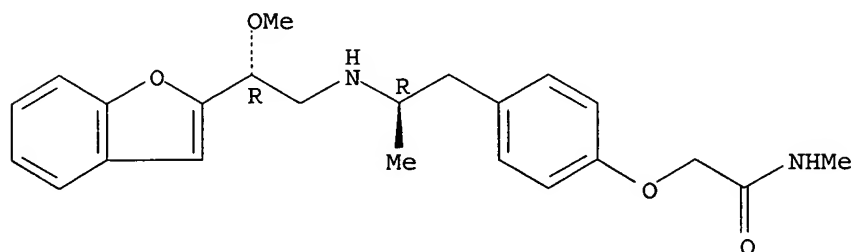
●2 HCl



RN 90469-93-5 HCAPLUS

CN Acetamide, 2-[4-[2-[[2-(2-benzofuranyl)-2-methoxyethyl]amino]propyl]phenoxy]-N-methyl-, dihydrochloride, (R\*,R\*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.

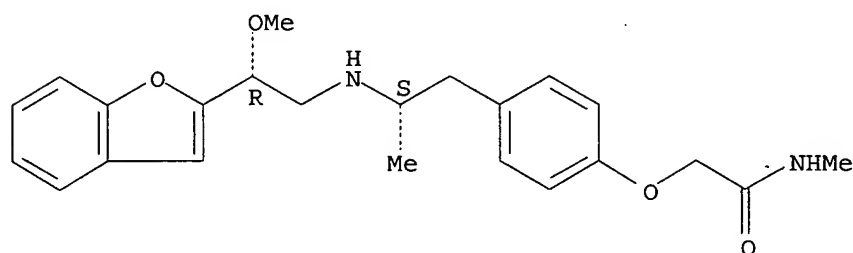


● 2 HCl

RN 90469-94-6 HCAPLUS

CN Acetamide, 2-[4-[2-[[2-(2-benzofuranyl)-2-methoxyethyl]amino]propyl]phenoxy]-N-methyl-, dihydrochloride, (R\*,S\*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.

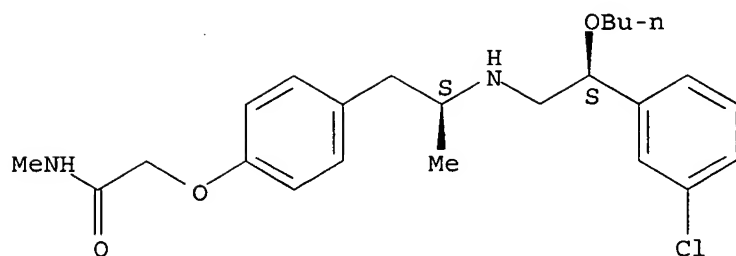


● 2 HCl

RN 90470-10-3 HCAPLUS

CN Acetamide, 2-[4-[2-[[2-butoxy-2-(3-chlorophenyl)ethyl]amino]propyl]phenoxy]-N-methyl-, monohydrochloride, (R\*,R\*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.

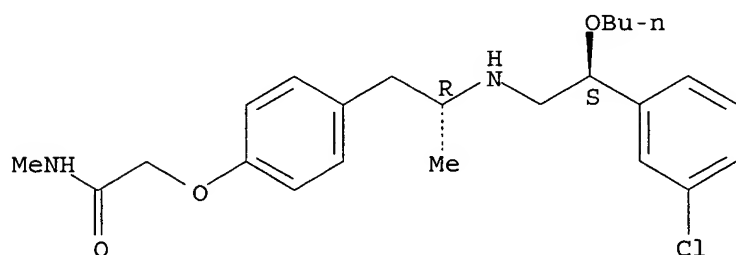


● HCl

RN 90470-11-4 HCAPLUS

CN Acetamide, 2-[4-[2-[[2-butoxy-2-(3-chlorophenyl)ethyl]amino]propyl]phenoxy]-N-methyl-, monohydrochloride, (R\*,S\*)- (9CI) (CA INDEX NAME)

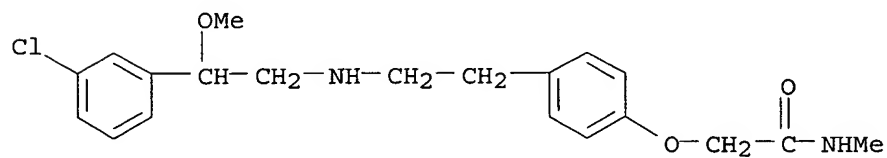
Relative stereochemistry.



● HCl

RN 90470-31-8 HCAPLUS

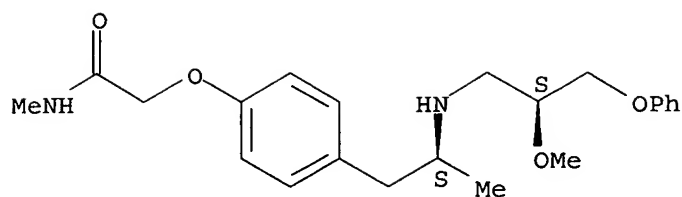
CN Acetamide, 2-[4-[2-[[2-(3-chlorophenyl)-2-methoxyethyl]amino]ethyl]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



RN 90470-34-1 HCAPLUS

CN Acetamide, 2-[4-[2-[[2-methoxy-3-phenoxypropyl]amino]propyl]phenoxy]-N-methyl-, monohydrochloride, (R\*,R\*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.

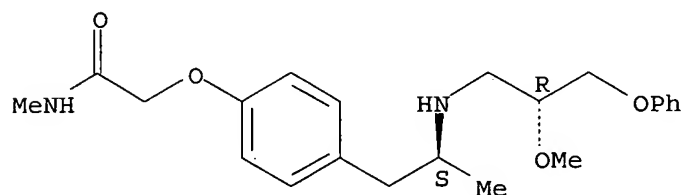


● HCl

RN 90470-35-2 HCAPLUS

CN Acetamide, 2-[4-[2-[(2-methoxy-3-phenoxypropyl)amino]propyl]phenoxy]-N-methyl-, monohydrochloride, (R\*,S\*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.

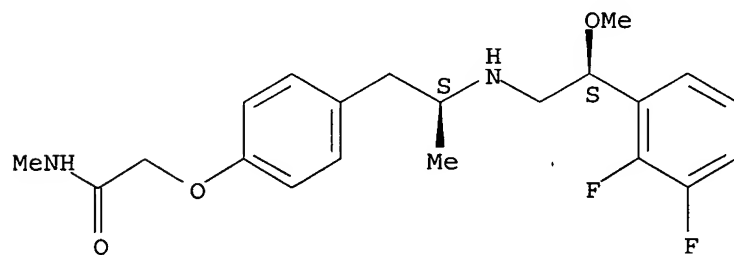


● HCl

RN 90470-40-9 HCAPLUS

CN Acetamide, 2-[4-[2-[[2-(2,3-difluorophenyl)-2-methoxyethyl]amino]propyl]phenoxy]-N-methyl-, (R\*,R\*)- (9CI) (CA INDEX NAME)

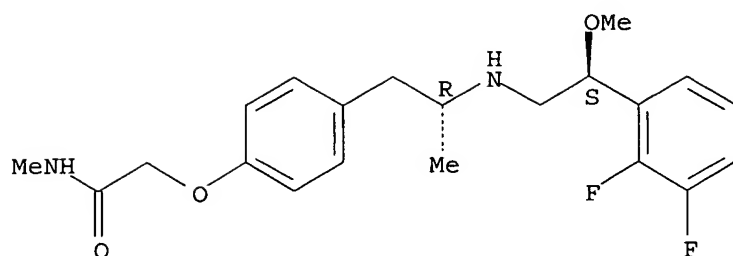
Relative stereochemistry.



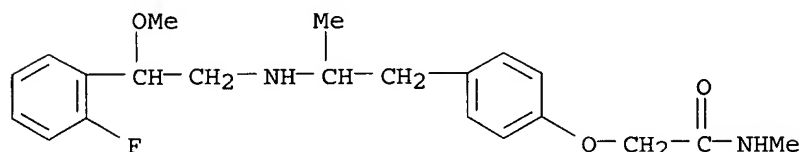
RN 90470-41-0 HCAPLUS

CN Acetamide, 2-[4-[2-[[2-(2,3-difluorophenyl)-2-methoxyethyl]amino]propyl]phenoxy]-N-methyl-, (R\*,S\*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



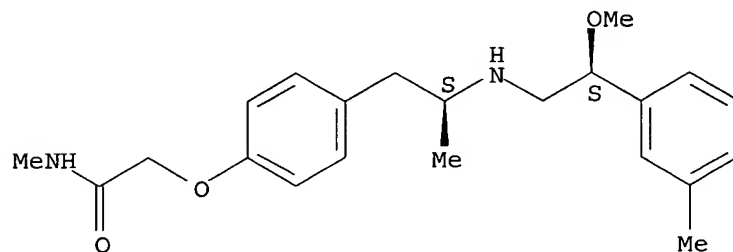
RN 90470-42-1 HCAPLUS  
 CN Acetamide, 2-[4-[2-[[2-(2-fluorophenyl)-2-methoxyethyl]amino]propyl]phenoxy]-N-methyl-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 90470-44-3 HCAPLUS  
 CN Acetamide, 2-[4-[2-[[2-methoxy-2-(3-methylphenyl)ethyl]amino]propyl]phenoxy]-N-methyl-, monohydrochloride, (R\*,R\*)- (9CI) (CA INDEX NAME)

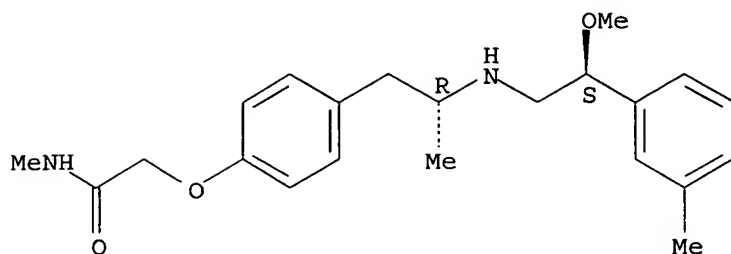
Relative stereochemistry.



● HCl

RN 90470-45-4 HCAPLUS  
 CN Acetamide, 2-[4-[2-[[2-methoxy-2-(3-methylphenyl)ethyl]amino]propyl]phenoxy]-N-methyl-, monohydrochloride, (R\*,S\*)- (9CI) (CA INDEX NAME)

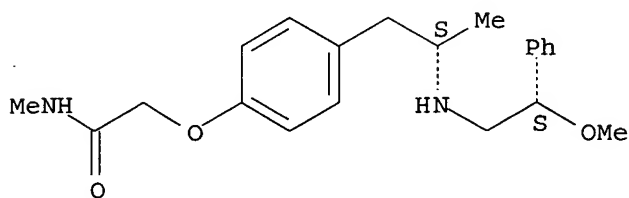
Relative stereochemistry.



● HCl

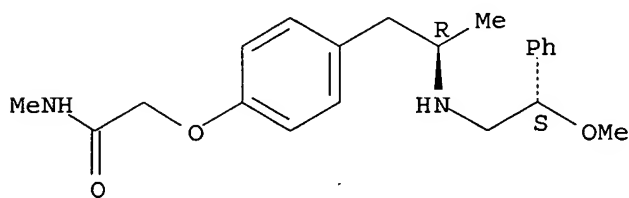
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 (preparation and hydride reduction of)  
 RN 90469-24-2 HCAPLUS  
 CN Acetamide, 2-[4-[2-[(2-methoxy-2-phenylethyl)amino]propyl]phenoxy]-  
 N-methyl-, (R\*,R\*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



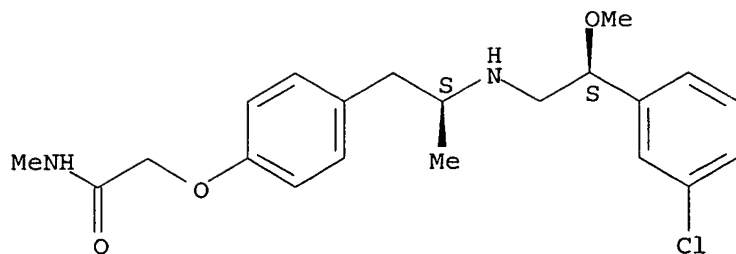
RN 90469-25-3 HCAPLUS  
 CN Acetamide, 2-[4-[2-[(2-methoxy-2-phenylethyl)amino]propyl]phenoxy]-  
 N-methyl-, (R\*,S\*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



IT 90469-09-3P 90469-10-6P 90469-36-6P  
 90469-37-7P 90469-40-2P 90469-41-3P  
 90469-55-9P 90470-75-0P 90470-76-1P  
 90486-20-7P  
 (preparation and reduction of, by borane)  
 RN 90469-09-3 HCAPLUS  
 CN Acetamide, 2-[4-[2-[[2-(3-chlorophenyl)-2-  
 methoxyethyl]amino]propyl]phenoxy]-N-methyl-, (R\*,R\*)- (9CI) (CA  
 INDEX NAME)

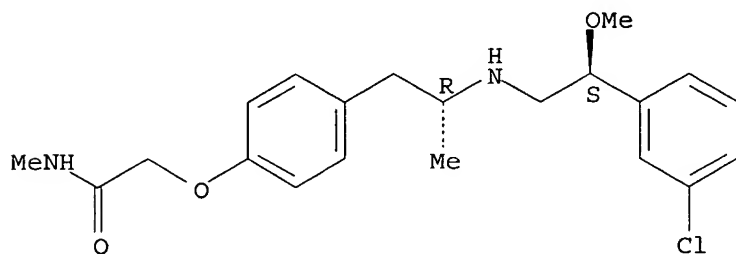
Relative stereochemistry.



RN 90469-10-6 HCAPLUS

CN Acetamide, 2-[4-[2-[[2-(3-chlorophenyl)-2-methoxyethyl]amino]propyl]phenoxy]-N-methyl-, (R\*,S\*)- (9CI) (CA INDEX NAME)

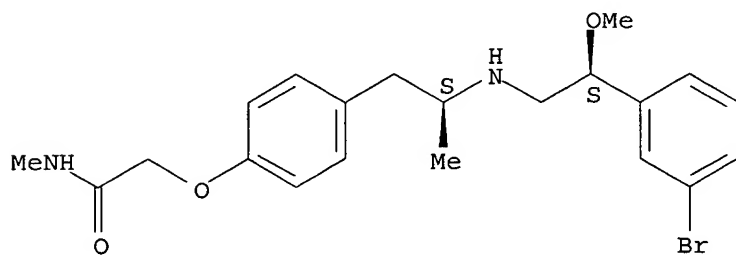
Relative stereochemistry.



RN 90469-36-6 HCAPLUS

CN Acetamide, 2-[4-[2-[[2-(3-bromophenyl)-2-methoxyethyl]amino]propyl]phenoxy]-N-methyl-, (R\*,R\*)- (9CI) (CA INDEX NAME)

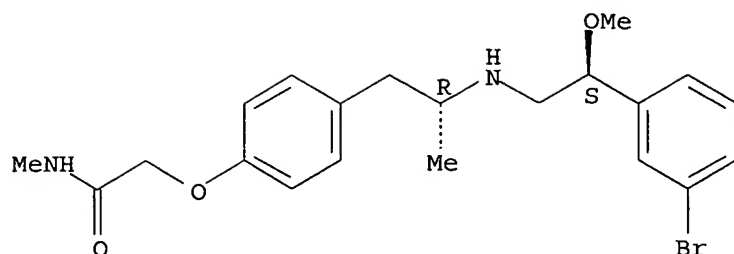
Relative stereochemistry.



RN 90469-37-7 HCAPLUS

CN Acetamide, 2-[4-[2-[[2-(3-bromophenyl)-2-methoxyethyl]amino]propyl]phenoxy]-N-methyl-, (R\*,S\*)- (9CI) (CA INDEX NAME)

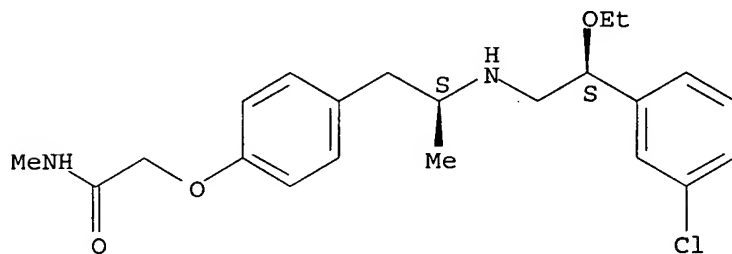
Relative stereochemistry.



RN 90469-40-2 HCAPLUS

CN Acetamide, 2-[4-[2-[[2-(3-chlorophenyl)-2-ethoxyethyl]amino]propyl]phenoxy]-N-methyl-, (R\*,R\*)- (9CI) (CA INDEX NAME)

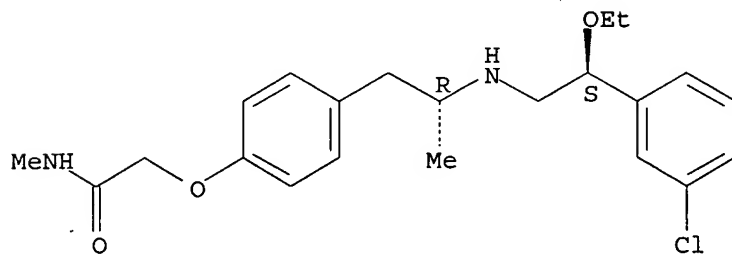
Relative stereochemistry.



RN 90469-41-3 HCAPLUS

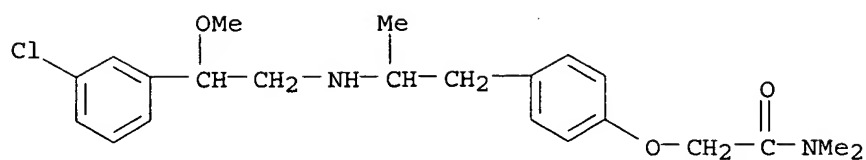
CN Acetamide, 2-[4-[2-[[2-(3-chlorophenyl)-2-ethoxyethyl]amino]propyl]phenoxy]-N-methyl-, (R\*,S\*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 90469-55-9 HCAPLUS

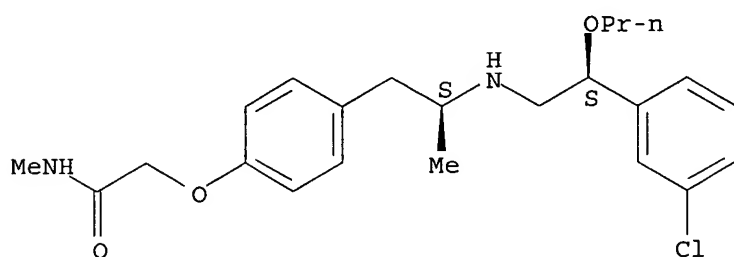
CN Acetamide, 2-[4-[2-[[2-(3-chlorophenyl)-2-methoxyethyl]amino]propyl]phenoxy]-N,N-dimethyl-, (9CI) (CA INDEX NAME)



RN 90470-75-0 HCAPLUS

CN Acetamide, 2-[4-[2-[[2-(3-chlorophenyl)-2-propoxyethyl]amino]propyl]phenoxy]-N-methyl-, (R\*,R\*)- (9CI) (CA INDEX NAME)

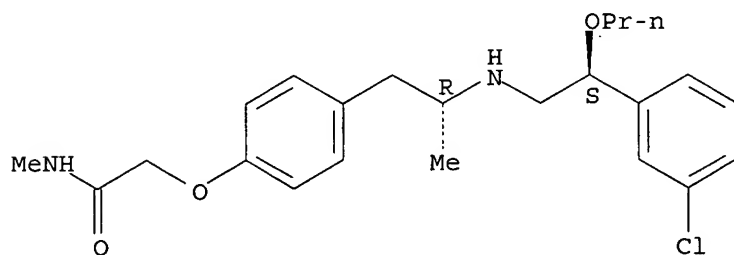
Relative stereochemistry.



RN 90470-76-1 HCAPLUS

CN Acetamide, 2-[4-[2-[[2-(3-chlorophenyl)-2-propoxyethyl]amino]propyl]phenoxy]-N-methyl-, (R\*,S\*)- (9CI) (CA INDEX NAME)

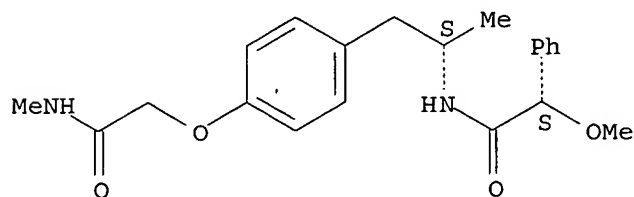
Relative stereochemistry.



RN 90486-20-7 HCAPLUS

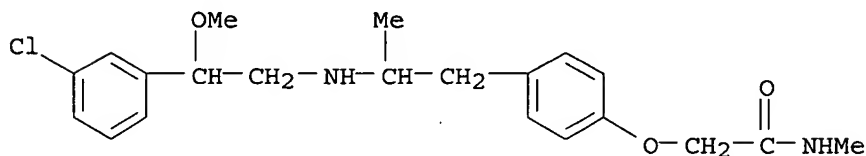
CN Benzeneacetamide, α-methoxy-N-[1-methyl-2-[4-[2-(methylamino)-2-oxoethoxy]phenyl]ethyl]-, (R\*,R\*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.





IT 90469-04-8P  
 (preparation of)  
 RN 90469-04-8 HCAPLUS  
 CN Acetamide, 2-[4-[2-[[2-(3-chlorophenyl)-2-methoxyethyl]amino]propyl]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



IC C07C093-04; C07C093-10; C07C093-14; C07C103-34; C07C103-178;  
 C07C101-42; C07C101-16; C07C149-42; A61K031-16  
 CC 25-4 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)  
 Section cross-reference(s): 1  
 ST phenethylamine phenylisopropyl prepn hypoglycemic;  
 phenylisopropylphenethylamine prepn hypoglycemic; antiinflammatory  
 phenylisopropylphenethylamine prepn; **antidiabetic**  
 phenylisopropylphenethylamine prepn; blood platelet  
 phenylisopropylphenethylamine prepn  
 IT **Antidiabetics** and Hypoglycemics  
 Inflammation inhibitors and Antiarthritics  
 (N-(phenylalkyl)phenethylamines)  
 IT 90468-92-1P 90468-92-1P 90468-93-2P 90468-96-5P  
 90468-97-6P 90469-01-5P 90469-02-6P **90469-03-7P**  
 90469-07-1P 90469-08-2P **90469-11-7P**  
**90469-12-8P** 90469-13-9P 90469-14-0P 90469-15-1P  
 90469-16-2P **90469-17-3P 90469-18-4P**  
 90469-19-5P 90469-20-8P 90469-22-0P 90469-23-1P  
**90469-30-0P 90469-31-1P 90469-32-2P**  
**90469-33-3P** 90469-34-4P 90469-35-5P 90469-38-8P  
 90469-39-9P **90469-42-4P 90469-43-5P**  
 90469-46-8P 90469-47-9P **90469-50-4P**  
**90469-51-5P** 90469-54-8P 90469-56-0P 90469-57-1P  
 90469-60-6P 90469-61-7P 90469-63-9P 90469-64-0P  
**90469-66-2P 90469-67-3P 90469-70-8P**  
**90469-71-9P** 90469-76-4P 90469-77-5P 90469-78-6P  
 90469-79-7P 90469-80-0P 90469-81-1P 90469-82-2P  
 90469-83-3P 90469-84-4P 90469-85-5P 90469-86-6P  
 90469-87-7P 90469-90-2P 90469-91-3P **90469-93-5P**  
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**90470-41-0P 90470-42-1P 90470-44-3P**  
**90470-45-4P** 90470-46-5P 90470-47-6P 90470-49-8P  
 90470-50-1P 90470-74-9P 90934-14-8P 93091-05-5P  
 (preparation and **antidiabetic** activity of)  
 IT 13031-13-5P 33224-88-3P 33225-01-3P **90469-24-2P**  
**90469-25-3P** 90469-44-6P 90470-53-4P 90470-54-5P

90470-57-8P 90470-59-0P 90470-61-4P 90470-63-6P  
 90470-65-8P 90470-68-1P 90470-70-5P 90470-71-6P  
 90486-21-8P

(preparation and hydride reduction of)

IT 90469-09-3P 90469-10-6P 90469-36-6P  
 90469-37-7P 90469-40-2P 90469-41-3P  
 90469-55-9P 90469-58-2P 90469-59-3P 90469-88-8P  
 90469-89-9P 90470-75-0P 90470-76-1P  
 90486-20-7P

(preparation and reduction of, by borane)

IT 90468-99-8P 90469-00-4P 90469-04-8P 90469-26-4P  
 90469-27-5P 90469-48-0P 90469-49-1P 90470-03-4P  
 90470-04-5P

(preparation of)

L32 ANSWER 38 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1981:461726 HCAPLUS

DOCUMENT NUMBER: 95:61726

TITLE: Ethanamine derivatives and their use in  
 pharmaceutical compositions

INVENTOR(S): Ainsworth, Anthony Trevor; Smith, David Glynn

PATENT ASSIGNEE(S): Beecham Group Ltd., UK

SOURCE: Eur. Pat. Appl., 46 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. -----	KIND ----	DATE -----	APPLICATION NO. -----	DATE
EP 23385	A1	19810204	EP 1980-301927	1980 0609
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EP 23385	B1	19821215		
R: AT, BE, CH, DE, FR, GB, IT, NL, SE				
US 4338333	A	19820706	US 1980-157555	1980 0609
<--				
AT 1994	E	19821215	AT 1980-301927	1980 0609
<--				
CA 1150297	A1	19830719	CA 1980-353754	1980 0611
<--				
DK 8002565	A	19801217	DK 1980-2565	1980 0613
<--				
AU 8059307	A1	19810108	AU 1980-59307	1980 0613
<--				
AU 533432	B2	19831124		
JP 56005444	A2	19810120	JP 1980-81268	

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0616

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ZA 8003576B4  
A19880531  
19810624

ZA 1980-3576

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ES 492489

A1

19810801

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&lt;--

ES 499604

A1

19820201

ES 1981-499604

1981  
0219

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PRIORITY APPLN. INFO.:

GB 1979-21038

A

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0616

&lt;--

EP 1980-301927

A

1980  
0609

&lt;--

OTHER SOURCE(S):  
GI

MARPAT 95:61726



AB HOCHRCH2NHCR1R2XX1OX2CO2H (R = optionally-substituted Ph; R1 = H, F, Cl, Me, OMe, OH; R2 = H, Me; X = bond, alkylene; X1 = phenylene, oxyphenylene; X2 = alkylene) were prepared. Thus, 4-MeO2CCH2OC6H4CHO was treated with EtNO2 to give 4-MeO2CCH2OC6H4CH:CHMeNO2 which was hydrogenated to 4-MeO2CCH2OC6H4CH2CMe:NOH. Hydrolysis of the oxime gave 4-MeO2CCH2OC6H4CH2COMe which was treated with 4,3-HO(HOCH2)C6H3CH(OH)CH2NH2 and hydrogenated to give I as a mixture of diastereoisomers. At 11 mg/kg orally in rats daily 28 days I decreased the lipid content from 18.6 to 12.9 g.

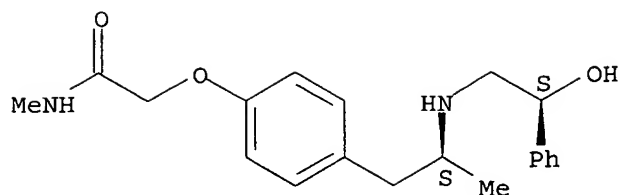
IT 78069-35-9P 78069-36-0P

(preparation and pharmacol. activity of)

RN 78069-35-9 HCAPLUS

CN Acetamide, 2-[4-[2-[(2-hydroxy-2-phenylethyl)amino]propyl]phenoxy]-N-methyl-, (R\*,R\*)- (9CI) (CA INDEX NAME)

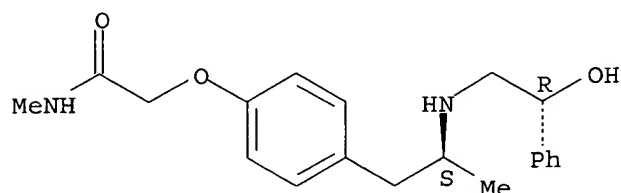
Relative stereochemistry.



RN 78069-36-0 HCAPLUS

CN Acetamide, 2-[4-[2-[(2-hydroxy-2-phenylethyl)amino]propyl]phenoxy]-N-methyl-, (R\*,S\*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



IC C07C093-14; C07C103-178; C07C103-34; A61K031-19

CC 25-4 (Noncondensed Aromatic Compounds)

ST phenylethanolamine phenylalkyl; obesity phenylethanolamine; antidiabetic phenylethanolamine

IT **Antidiabetics** and Hypoglycemics  
(phenylethanolamine derivs.)

IT 78069-20-2P 78069-21-3P 78069-23-5P 78069-29-1P

78069-30-4P 78069-31-5P 78069-32-6P 78069-33-7P

78069-34-8P **78069-35-9P 78069-36-0P**

86615-96-5P

(preparation and pharmacol. activity of)